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RETINAL CHANGES ASSOCIATED WITH DIABETES AND WITH HYPERTENSION

A COMPARISON AND CONTRAST

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The significance of the ophthalmoscopic changes associated with diabetes and with hypertension is of perennial interest. There is still controversy as to the existence of a specific diabetic retinopathy. Some authorities, impressed by the undeniable resemblances between the retinal changes associated wth diabetes and those accompanying hypertension, the rarity of such changes in young diabetic patients and the relative frequency of retinopathy in diabetic persons with hypertension, are satisfied that diabetic retinopathy is simply hypertensive, or even arteriosclerotic, retinitis somewhat modified by its appearance in a diabetic patient.

As one who takes the opposite view, I should like to present the picture of diabetic retinopathy as an entity by comparing and contrasting the lesions of this disorder with lesions associated with hypertension.

The fundus picture of diabetes and that of hypertension are composed of the same elements —vascular changes, hemorrhages and exudates— and superficially are somewhat similar, but closer examination shows that in form, distribution and evolution these components of the picture present characteristic differences. The admitted resemblances suggest that there must be some common factor in their pathogenesis, but even in cases of moderately advanced stages of the two types of retinopathy one can note certain differences, and a survey of a wide range of clinical material leads one to two convictions: first, that diabetic and hypertensive retinopathy are two separate clinical and pathologic entities, and, second, that the current descriptions of diabetic retinopathy are inadequate.

In the textbook illustrations of the diabetic fundus hemorrhages tend at first to be confined to the macular and papillomacular areas and take the form of dots and blots. In the later stages the hemorrhages are more widespread, and the "blots" predominate; in other words, the hemorrhages are larger and darker and of irregular shape. Some may be of the ill defined, mossy type, while others are sharply outlined and give the impression of being superficial, under the internal limiting membrane, or even subhyaloid.

The exudates are also situated primarily in the central area and consist of small white dots, which tend to coalesce and form irregular waxy, yellowish white patches, with a fine dark outline. Finally, changes in the vessels, if present, affect principally the veins. The arteries often show little or no abnormality, and there may be notable absence of diffuse edema of the papilla and the retina.

In the retina of a patient with hypertension the hemorrhages occur first near the disk and form streaked, spindle-shaped or flamelike patches, radiating from the margin of the disk and obviously located in the nerve fiber layer. Sometimes they can be related more closely to the arteries than to the veins.

The exudates are of two kinds—round white, cotton wool patches, the size of a quarter of the disk to that of the disk, and even larger, which often cover and conceal the blood vessels; and discrete, grayish white dots, which group themselves in constellations or, in the center of the fundus, form rows of more or less confluent spots radiating from the macula as the so-called macular star.

With these lesions are vascular changes which characteristically affect the arteries. When arteriosclerosis is not an important factor, as in younger hypertensive persons and in pregnant women, the arteries show diffuse spastic contraction. In arteriosclerotic subjects the arteries present variations in caliber, a copper wire or silver wire appearance, and possibly sheathing. The veins play a purely passive role, the changes being limited to the appearance of narrowing, depression and deflection when they are crossed by the arteries. In patients with malignant hypertension papilledema is often sufficiently

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striking to suggest the existence of an intracranial neoplasm.

It goes without saying that neither with diabetes nor with hypertension will one picture serve for every case. The changes which I have described may be called typical, of moderate severity, but with both conditions there is a good deal of variation from one case to another.

The view of investigators who assert the identity or close relation of diabetic and hypertensive retinopathy is based on the similarity of the fundus pictures; the alleged frequent association of arteriosclerotic changes and of general arterial hypertension with diabetes; the lack of recognizable correlation of the retinopathy with such factors as the severity of the diabetes, the age of onset and the duration of the disease, and the rarity of retinal changes in young diabetic patients and their more characteristic occurrence with diabetes in elderly subjects. But against this argument one must admit the real differences between the diabetic and the hypertensive fundus; the fact that of a large series of diabetic patients subjected to ophthalmoscopic examination, over 50 per cent with retinal changes had no abnormality of blood pressure; the frequent absence of arteriosclerotic changes in the retina of diabetic patients, and, as will be seen, the difference in mode of onset, development and termination of the changes in the retina.

Although diabetic retinitis is uncommon in the very young, it occurs in the middle-aged rather than in the elderly and is occasionally seen in the second decade. (The youngest patient in my own experience was a lad 19 years of age.) Moreover, the fact that retinopathy of hypertension has a much more serious bearing on the prognosis *quoad vitam* than has the retinopathy of diabetes mellitus indicates an important difference in the pathology of the two conditions.

In the hypertensive disease, one can, to some extent, relate the varieties of the fundus picture to recognized clinical groups, such as senile atherosclerosis, generalized arteriosclerosis, chronic glomerulonephritis, benign hypertension, malignant hypertension and the toxemia of pregnancy. In diabetes, on the other hand, although the ophthalmoscopic picture shows wide variations, one cannot claim to be able to correlate these variations with any such clinical grouping. The absence of discoverable correlation between the retinopathy of diabetes and such factors as age, duration and severity of the disease, blood pressure and peculiarities of the blood and urine does not appear to help my argument; but it is evident that the comparatively low incidence of retinal changes associated with diabetes, as well as the wide variation in these changes when they do occur, must depend on biochemical differences not yet discovered, or even suspected.

The current descriptions of diabetic retinopathy make too little of the overfilling of the retinal veins, which, since it has often been observed as the only visible abnormality, is probably an important early sign, or at least a diagnostic hint. In about one-third the patients with diabetes subjected to routine ophthalmoscopic examination in the Tennent Institute my associates and I have found the retinal veins enlarged and tortuous, and on more than one occasion the discovery of this change in the course of ophthalmoscopic examination in medical patients has led us to hazard a diagnosis of diabetes and this guess has been confirmed.

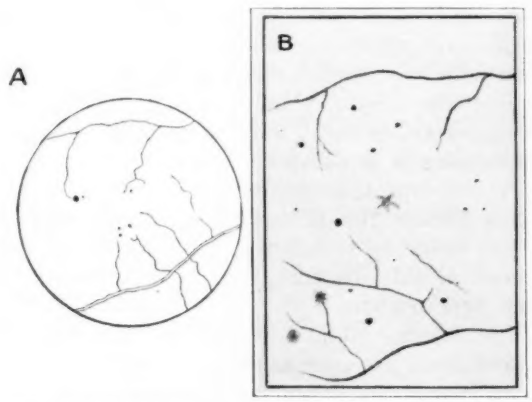

Fig. 1.—*A*, microaneurysms in the perimacular area, and, *B*, microaneurysms and punctate hemorrhages in the central area of the fundus, in a case of diabetes.

Prof. A. Loewenstein informed me that in examination of the fundi of 15 diabetic children, 5 to 16 years of age, dilatation of the veins without any other anomaly was noted in 6 patients. In view of the accumulating evidence that the vascular changes in diabetic retinopathy tend to affect the venous, rather than the arterial, side of the circulation, this sign should be borne in mind as early evidence of stasis in the venous circulation of the retina.

A more important phenomenon, although of less frequent occurrence, is the appearance of minute globular aneurysms on the retinal capillaries, usually discovered singly or in small numbers within or near the macular area. The occurrence of these microaneurysms in such a situation and without other changes in the fundus we believe to be the earliest unequivocal sign of diabetes (fig. 1 *A* and *B*).

In a communication to the Ophthalmological Society of the United Kingdom, in 1943, Prof. A. Loewenstein and I,[1] referring to the so-called punctate hemorrhages of diabetic retinitis, gave reasons for the belief that at least some of them —small, round and situated on or near the small perimacular vessels—were actually capillary aneurysms; further histologic study has confirmed this view and made clear the distinction between true punctate hemorrhages and microaneurysms. In diameter the latter are not much larger than the perimacular vascular twigs, say 50 to 60 microns. They are perfectly round, and

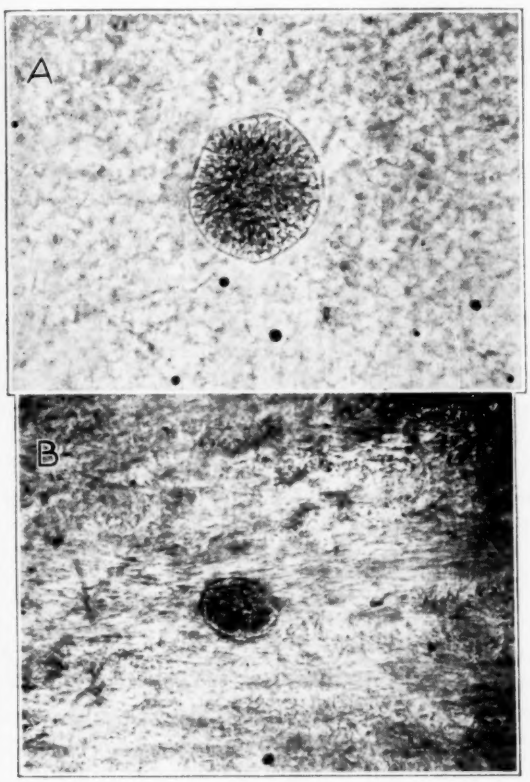

Fig. 2.—Unstained retinas in bulk, viewed flat, in a case of diabetes, showing (*A*) a thin-walled microaneurysm with parent capillary and (*B*) a microaneurysm with thickened wall.

their globular form is sometimes indicated by the presence of a bright central reflex.

If the posterior segment of the eye, in which these aneurysms are present, is fixed in a dilute solution of formaldehyde and examined with the loupe or with the slit lamp and corneal microscope, the aneurysms can be clearly seen in greater numbers than on ophthalmoscopic examination. In bulk specimens of the retina examined flat and in stained sections with higher magnification microaneurysms are observed to be still more numerous.

In the unstained retina, mounted in glycerin and viewed flat, the aneurysm appears as a mulberry-like body composed of a compact mass of erythrocytes enclosed in a membrane of varying thickness—in some cases a thin, structureless film and in others a wall of some thickness, which may have a fibrillary character (figs. 2 *A* and *B* and 3 *a*).

In favorable cases, that is when the retinal capillaries are filled with blood, it can be shown that the aneurysms occur in the course of the capillaries at a level deeper than that of the principal retinal vessels (figs. 2 *A* and 3). In stained sections of the retina, cut both horizontally (fig. 4 *A*) and vertically (fig. 4 *B*), these characters are verified, and it can be seen that,

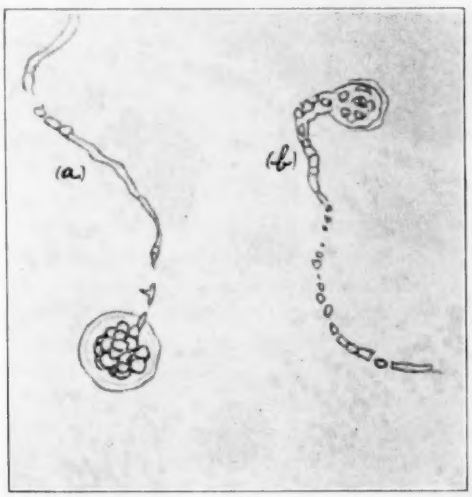

Fig. 3.—Unstained retina in bulk, viewed flat, showing microaneurysms with capillary attached.

with few exceptions, the aneurysms are situated in the inner nuclear layer and are globular distentions of the capillaries which form a link between the first capillary plexus, in the ganglion cell layer, and the deeper plexus situated at the outer boundary of the inner nuclear layer; that is, the aneurysms are situated between the precapillaries on the arterial side and those on the venous side of the retinal circulation. They are usually distinguished easily from hemorrhages by their spherical form, by their definite limiting wall, sometimes composed of recognizable endothelial cells, and by their situation. Hemorrhages, which may occur at any depth, are often round or oval in individual sections and may thus be mistaken for aneurysms, but in serial sections are seen to have no containing wall and to infiltrate the different layers of the retina in an irregular fashion.

1. Ballantyne, A. J., and Loewenstein, A.: Tr. Ophth. Soc. U. Kingdom **63**:95, 1943.

Berens [2] described the fundus of a diabetic patient, in which, together with other lesions, such as hemorrhages, exudates and abnormalities of the larger vessels, a large number of telangiectases were present. These were undoubtedly aneurysmal; but they differed from the microaneurysms previously referred to, first, in their larger size and, second, in their obvious attachment to the visible vessels. The microaneurysms are often of pinpoint size, and although they sometimes appear to be attached to the fine perimacular vessels in the ophthalmoscopic view, microscopic study shows that they occur in the course of the capillaries and are situated in the inner nuclear layer.

Fig. 4.—*A*, retinal section cut horizontally, showing microaneurysm in the nerve fiber layer; *B*, retina in vertical section, showing microaneurysm in the inner nuclear layer.

It is not claimed that aneurysms of this type occur only with diabetes, for they occur, for example, with hypertension, especially as a sequel to thrombosis of a branch of the central retinal vein; but in this condition, and in other exceptional situations, they are more likely to be seen outside the limits of the area centralis and are always associated with obvious vascular changes and with hemorrhages of the grosser type.

It is the occurrence of these microaneurysms in small numbers, in the central area of the fundus, either alone or with fine white specks or petechial hemorrhages, which produces an unfamiliar picture diagnostic of diabetes mellitus.

On account of their small size and the dark color of the perimacular background, the aneurysms are easily overlooked on ophthalmoscopic examination. It may be necessary to make an examination with a dilated pupil, and the use of a convergent or focused beam in the ophthalmoscope is helpful. Although the aneurysms are small, they are sharply defined, and this is no doubt due to their comparatively superficial position; many of the small hemorrhages which might be mistaken for aneurysms are in the outer molecular and outer nuclear layers and are therefore less sharply defined.

The position of the microaneurysms is of special importance in relation to the changes of diabetic retinopathy, for, situated as they are between the arterial and the venous side of the retinal circulation, they indicate that the initial pathologic change lies on the venous, rather than on the arterial, side and provide strong support for the view, expressed by Mylius [3] and other authors, that venous stasis is an early and essential factor in the development of diabetic retinopathy.

The formation of the capillary aneurysms seems to require the operation of two factors: weakening of the resistance of the capillary walls and a relative increase of pressure within the vessel. Both in unstained specimens of the retina in bulk and in stained sections, I have noted what appears to be a very early change in the capillaries, namely, swelling of the endothelial cells, causing partial or complete blockage of the lumen; and in suitably prepared specimens fatty granules can be seen in the endothelium. I believe that the damaged endothelial cells are less resistant than the normal cells and that when there is a more or less complete block on the venous side, the capillary walls yield to the endovascular pressure. Stasis of the blood stream will itself cause further damage to the endothelium, and so a vicious circle may be established. In veins of more than capillary size I have noted a special tendency to the presence of fatty deposits in the endothelium at junctions and bifurcations and to the formation of saccular aneurysms at such points.

2. Berens, C.: Aging Process in Eye and Adnexa, Arch. Ophth. **29**:171 (Feb.) 1943.

3. Mylius: Klin. Monatsbl. f. Augenh. **98**:377, 1937.

It should be noted that in cases of hypertension, also, fatty droplets are noted in the smaller retinal arteries, but in that condition the fatty droplets tend to form in the middle and outer layers of the wall, rather than in the endothelium.

The diameter of the microaneurysms may be as much as ten or fifteen times that of the parent capillary, and it is therefore not surprising that the wall is often stretched so thin as to be scarcely recognizable; nor is it surprising that blood is thus permitted to escape by diapedesis or by rupture. In the unstained retina in bulk one occasionaly sees a ruptured aneurysm asso-

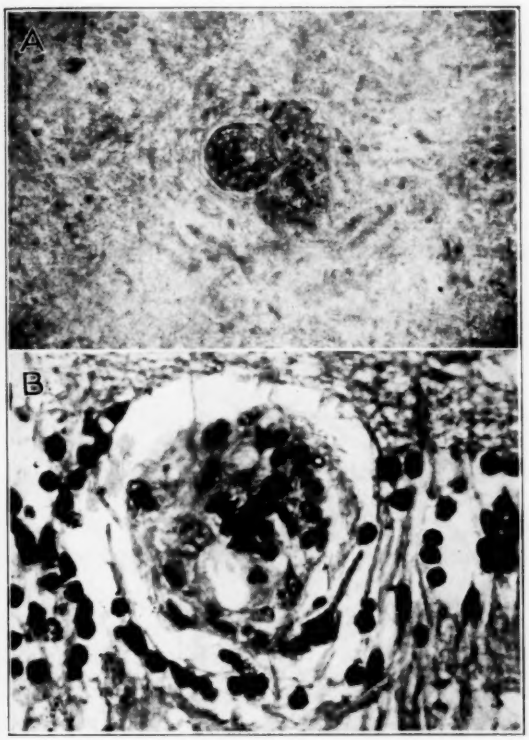

Fig. 5.—*A*, unstained retina in bulk, viewed flat, showing hemorrhage from a microaneurysm; *B*, retina in vertical section in a case of diabetes, showing microaneurysm in the inner nuclear layer, which has become thrombosed.

ciated either with staining of the surrounding tissue with hemoglobin or with an extravasation of erythrocytes (fig. 5 *A*). In the ophthalmoscopic view, also, one may occasionally see a small round aneurysm conjoined with an irregularly shaped petechial hemorrhage.

It has been mentioned that some of the aneurysms are enclosed in a thick wall of hyaline or fibrillary character. This capsule might be the result of a proliferative reaction on the part of the local glial tissue. One would expect such a wall to be more or less opaque and to correspond with the ophthalmoscopic appearance of a white dot. In 1 or 2 instances I have seen a microaneurysm in the fundus becoming surrounded by a pale halo, which encroached on the red area and became increasingly pale until the red spot was completely replaced by a white one. I have no proof of the identity of these ophthalmoscopic lesions, but the point deserves further observation.

Another histologic change which may have bearing on this question is that of swelling of the capillary endothelium, thrombosis of the aneurysm and subsequent cicatrization (fig. 5 *B*). Staining with scarlet red sometimes reveals the presence of fat in such a lesion. This, also, might be expected to appear under the ophthalmoscope as a white dot. As a matter of fact, in cases in which the diabetic "exudates" are still punctate it is often possible to distinguish certain small discrete round specks from others which are of more variable size and shape and which tend to coalesce to form larger dots or patches. The former seem to correspond with the thrombosed and fatty aneurysms previously referred to.

I have dealt at some length with these capillary aneurysms because they appear to have escaped notice and because, since they are probably the earliest visible manifestation of diabetic retinopathy, they should throw some light on the pathogenesis of that condition.

The only histologic event which seems to precede their formation is the swelling of the endothelium of the capillaries and precapillaries in association with the deposit of fatty granules within their walls.

There is a considerable gap, both ophthalmoscopically and histologically, between this minimal form of diabetic retinopathy and another, hitherto little known, type, in which the outstanding feature is the presence of notable changes in the larger retinal veins.

Enlargement and beading of the veins in cases of diabetes were demonstrated by Nettleship,[4] in 1888, and more recent references have been made by Gray,[5] Braun,[6] Bonnet and Bonamour,[7] O'Brien and Allen,[8] Agatston[9] and Gibson and

4. Nettleship, E.: Tr. Ophth. Soc. U. Kingdom **8**:159, 1888.

5. Gray, W. A.: Brit. J. Ophth. **17**:577, 1933.

6. Braun, R.: Zentralbl. f. d. ges. Ophth. **38**:65, 1937.

7. Bonnet, P., and Bonamour, G.: Bull. Soc. d'opht. de Paris **5**:367, 1938.

8. O'Brien, C. S., and Allen, J. H.: Unusual Changes in Retinal Veins in Diabetes, Arch. Ophth. **24**:742 (Oct.) 1940.

9. Agatston, S. A.: Clinicopathologic Study of Diabetic Retinitis, Arch. Ophth. **24**:252 (Aug.) 1940.

Smith.[10] Most instructive are the illustrations in the paper of O'Brien and Allen, and the same changes are also represented in figures 6 *A* and *B* and 7).

The principal branches of the central retinal vein are full, tortuous and variable in caliber, but these changes are not of uniform distribution; they are limited to individual branches or to segments of branches. The tortuosity may be extreme and may take bizarre shapes; the variations in caliber usually take the form of intermittent expansions and may amount to actual beading, and the veins may be thrown into loops and coils. Together with these changes, one sometimes sees bunches or networks of "new-formed" veins of varying sizes, which histologic examination shows to be partly intraretinal and partly preretinal.

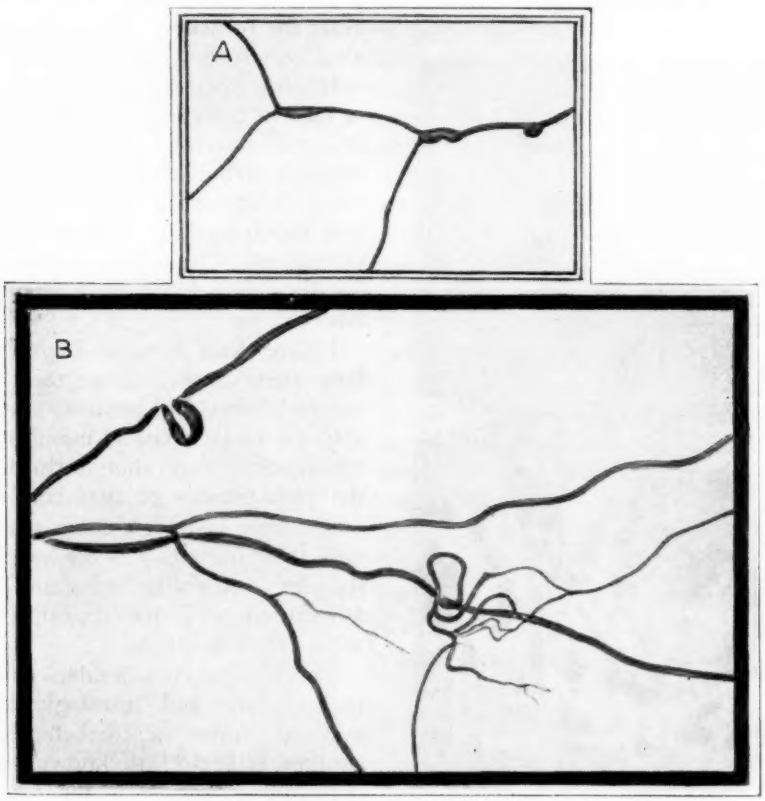

Fig. 6.—*A* and *B*, changes in the retinal veins in diabetes.

Networks of fine venules in and on the retina are not uncommon in cases of arteriosclerosis with thrombosis of a branch of the retinal vein; but leashes or networks of new vessels almost as large as the parent vessels rarely occur in such conditions, and the gross venous changes here illustrated are peculiar to diabetes. Like the capillary aneurysms, they suggest a state of stasis in the capillary and venous circulation; but the picture differs notably from that of thrombosis either of the trunk or of a branch of the central retinal vein. If the central vein is blocked behind the point of its division on or behind the disk, all the retinal branches are distended and tortuous, and hemorrhages are scattered all over the fundus, while if a principal division is obstructed all the vessels in one quadrant of the fundus are distended and abundant hemorrhages cover the same quadrant. In the conditions here described the changes in the vessels are strikingly erratic in their distribution, and hemorrhages may be few or absent.

Histologic examination of the vessels in this type of retinopathy shows a large variety of lesions, in keeping with the varied ophthalmoscopic changes. In general, the larger and the medium veins present a process of phlebosclerosis (fig. 8 *A*), with gross thickening of their walls, sometimes fibrillary, sometimes hyaline, and with this a formation of larger, thin-walled veins or dilated capillaries, sometimes forming networks within the retina, on its anterior surface (fig. 8 *B*), or even in the vitreous.

The retinal exudates in diabetes and in the hypertensive diseases present many unsolved

10. Gibson, G. G., and Smith, L. W.: Retinal Phlebosclerosis, Arch. Ophth. **26**:840 (Nov.) 1941.

problems. Ophthalmoscopically there is a certain resemblance between the white punctate exudates in these two conditions, but in diabetes they show a tendency to coalesce and form larger, waxy or lardaceous patches. Occasionally they group themselves in a circinate manner, but they do not simulate the macular star of "albuminuric retinitis." Study of sections shows that most of these punctate exudates are in the outer molecular layer. Their differentiation is not completely understood; but my material shows in the cases of diabetes rounded, solid, hyaline masses, while in cases of the hypertensive type the corresponding masses are sometimes wholly albuminoid, sometimes fibrinous and sometimes a combination of the two types with red blood corpuscles. Diffuse retinal exudates are not common with diabetes; but with the severer forms of hypertensive retinopathy there

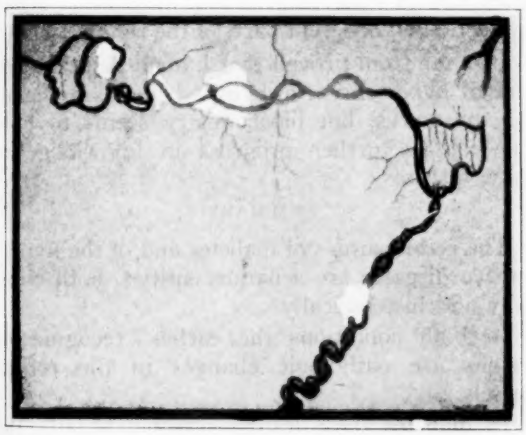

Fig. 7.—Gross changes in branches of the lower temporal vein in a case of diabetes.

is often a plasmoid infiltration of the nerve fiber layer and other layers, and subretinal plasmoid exudates are common. There is much still to be learned about the origin of the exudates and their chemical composition.

The most advanced intraocular changes observed in the diabetic eye are no less impressive than the changes I have been discussing. They are often accompanied by intraocular hemorrhages and exudates or by opacity of the lens, changes which make ophthalmoscopic examination impossible, so that the picture of the fundus must be obtained by examination of the excised and bisected eye. In its final phase the eye is blind and often painful, due to iritis or acute glaucoma. Retinitis proliferans, retinal detachment and retinal, preretinal and subretinal exudates and hemorrhages may all form part of the picture, and microscopic examination may show extreme examples of phlebosclerosis, new-formed blood vessels and cystic degeneration.

Throughout this description of the different varieties of diabetic retinopathy there has been the implicit assumption that they are stages in a sequence of pathologic changes, commencing with fatty infiltration and swelling of the endothelium of the smaller vessels and proceeding through capillary and venous stasis, the formation of capillary microaneurysms, phlebosclerosis, venous and capillary thrombosis, hemorrhage and exudate, to the complete disorganization of the eye. This may be true, but of course it lacks

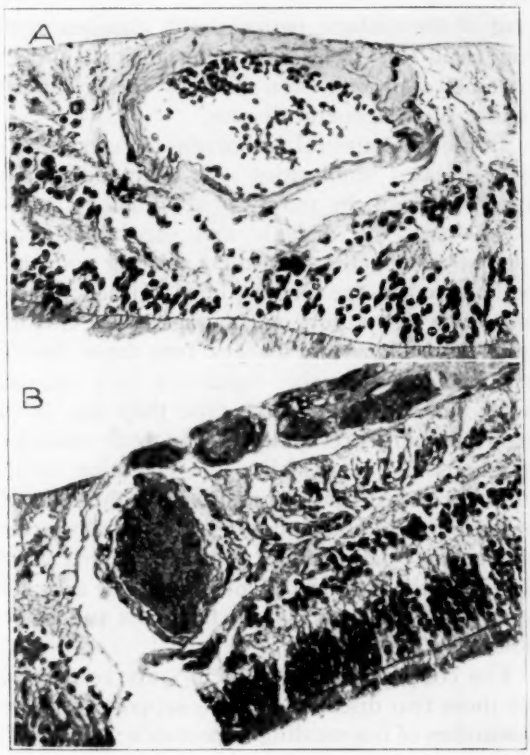

Fig. 8.—*A*, phlebosclerosis in a case of advanced diabetic retinopathy; *B*, a retinal vein which has perforated the internal limiting membrane and has led to the formation of a preretinal vascular plexus.

proof. We have never been in a position to follow any one case through all these stages, and since we cannot correlate the presence or absence or the intensity of these changes with the duration and severity of the diabetes, it is difficult to see how a clear proof is to be arrived at. But it may at least be considered that they give something like a true picture of the sequence of pathologic events.

The final degenerative phase is one which is seldom met with in cases of hypertension. The fact that the pathologic changes originate on the

arterial side of the retinal circulation must influence the character of the later developments, but it must not be forgotten that the most extreme changes in the diabetic eye can be found in a patient whose expectation of life is still relatively favorable, whereas the duration of life of the subject of hypertensive retinopathy is notoriously short and there is seldom time for such advanced degenerative changes to develop.

Enough has been said to show that whatever may be the superficial resemblances, the differences between diabetic and hypertensive retinopathy clearly support the view that they are two distinct entities. Admittedly, the two disorders may occur in one and the same patient—50 per cent of the diabetic patients with changes in the fundus in this series had hypertension—and the retinal condition often reflects the composite nature of the general disease.

In the fundamental pathologic changes in these two diseases similarities and differences again appear. From the purely ophthalmologic standpoint, both the diabetic and the hypertensive type of retinopathy have their starting point in a pathologic change in the finer retinal vessels; but always at a very early stage there is a difference in that in the diabetic type these changes are primarily in the capillaries and venules, while in the hypertensive type they are in the arterioles and precapillaries. In both disorders it is possible to visualize the evolution of the fully developed fundus picture from these simple beginnings. In both conditions the initial vascular change may be due to a chemical agent; but if this is so, the chemical agents must have a specific affinity, in the one case, for the veins and, in the other, for the arteries.

The concept that toxic factors are responsible for these two diseases receives support from two researches of outstanding importance: Goldblatt's experimental production of hypertension by occlusion of the renal arteries [11] and the demonstration by Dunn and associates [12] that pancreatic diabetes can be produced in experimental animals by the injection of alloxan (mesoxalyl urea).

The work of Goldblatt and his successors proved that experimental ischemia of the kidney brings about the formation of a toxic substance which causes lasting hypertension. In Dunn's experimental animals the injection of alloxan not only destroyed the islets of Langerhans and produced glycosuria, but, as Loewenstein [13] showed in Dunn's rabbits, caused diabetic cataract and the deposition of glycogen in the tissues of the eye. It has already been shown (Mori [14]) that glycogen occurs in the tissues of the human eye in cases of diabetes; Loewenstein confirmed this observation and failed to find glycogen in the human eye in cases of hypertension.

Incidentally, Dunn's work not only showed that pancreatic diabetes can be produced by chemical agents; it demonstrated, by the selective action of alloxan on the beta cells of the islets, how highly specific such chemical agents can be. Another striking illustration of such a selective action of chemical substances on different tissues is afforded by the fact that the pituitary body, with three different types of cells, is capable of producing a profound influence on the function of eleven different organs. It is therefore conceivable that toxic factors in diabetes and in hypertension may exercise a selective action on different parts of the retinal vessels.

It is far from proved that human diabetes and human hypertension are caused by toxic chemical substances, but biochemistry seems to hold the key to further progress in knowledge of these diseases.

SUMMARY

The retinopathies of diabetes and of the hypertensive diseases are separate entities, both clinically and histologically.

In both conditions the earliest recognizable lesions are pathologic changes in the retinal vessels.

In diabetes these lesions affect primarily the venous, and in hypertension the arterial, side of the retinal circulation.

In diabetes these changes point to venous stasis and, in addition to the familiar hemorrhages and exudates, consist of congestion of the veins, microaneurysms on the capillaries and gross changes in the principal veins.

Microaneurysms may occur alone and seem to be the earliest pathologic change in the fundus of the diabetic patient.

Histologically, the earliest recognizable change takes the form of minute fatty granules in the vascular endothelium, together with swelling of the endothelial cells. In hypertension fatty granules are observed more frequently in the media and the adventitia.

The most striking changes in the retinal veins of the diabetic patient appear as expansions, beading and the formation of loops, coils and networks, and the predominant histologic changes at this stage are phlebosclerosis and in-

11. Goldblatt, H.: J. Exper. Med. **67**:809, 1938.
12. Dunn, J.; Kirkpatrick, J.; McLetchie, N. G. B., and Telfer, S. V.: J. Path. & Bact. **55**:245, 1943.
13. Loewenstein, A.: Personal communication to the author.
14. Mori, S., abstracted, Zentralbl. f. d. ges. Ophth. **25**:141, 1931.

traretinal and preretinal networks of large, thin-walled vessels.

The hemorrhages in diabetic retinopathy occur primarily in the central area of the fundus, are characteristically rounded and occur chiefly in the deep layers, for the most part the internuclear layer.

In hypertension arterial changes predominate; the hemorrhages are primarily circumpapillary and striate, owing to their situation in the nerve fiber layer. Exudates are observed in the deep layers but also include patches of ganglioform degeneration in the nerve fiber layer.

It may be that in both forms of retinopathy toxic factors are responsible for the initial changes in the vessels, that these factors are, at least in part, specific to hypertension or to diabetes and that their selective action on the walls of the capillaries and the larger vessels accounts for the differentiation of the two forms of retinopathy.

11 Sandyford Place.

AN UNUSUAL TYPE OF KERATITIS ASSOCIATED WITH EXPOSURE TO N-BUTYL ALCOHOL (BUTANOL)

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We have recently had the opportunity of studying an unusual type of corneal lesion, presumably due to butanol (n-butyl alcohol), which affected a considerable proportion of the workers in a local rubber factory. The only previous report in the literature of ocular disturbances that may have had a similar cause is the description of conjunctivitis in 11 workers, 3 of whom had keratitis, employed in a straw hat factory where butyl alcohol and butyl acetate were used as solvents.[1] Ocular irritation has, however, been recently noted in five local factories in addition to the one here referred to, and a survey of all six outbreaks, showing the relation between butanol concentration in the air and the incidence of ocular irritation will shortly be published by Tabershaw, Fahey and Skinner.[2]

INDUSTRIAL BACKGROUND

The ocular disturbances with which this report is concerned occurred in a plant engaged in making Army raincoats. The manufacturing operation consisted of cutting the goods, stitching the buttonholes and cementing the sleeves, collars and pockets in place. The ocular disturbances occurred exclusively on the floor where the principal operation was cementing; no ocular disturbances occurred on the floors where the goods were handled but not cemented.

In the cementing process a synthetic resin paste and a volatile solvent were used. The paste was applied by the finger tips and the solvent by a sponge. Until one year ago methylethylketone had been used as the solvent. At that time a polyvinyl butyral resin, with different solubility characteristics, was introduced as the cement, and the solvent was changed temporarily to ethyl alcohol denatured with aviation gasoline. During this time there were no instances of ocular irritation. Two months ago the solvent was changed to butanol, to which diacetone alcohol and denatured alcohol were added in varying quantities, the amount depending on the weather. Only since this time has ocular irritation occurred to any abnormal degree.

The butanol vapor concentration of the air was determined in various sections of the department where the affected persons were stationed and was found to vary from 15 to 100 parts per million.[3] The maximum concentration corresponded to the area with the largest number of affected employees.

CLINICAL OBSERVATIONS

Incidence.—Approximately 75 girls were employed in the department where the ocular involvement occurred. Of these, 19 had complained to the dispensary nurse of ocular irritation within the few weeks just prior to our visit to the plant. Of these 19 girls, 17 had the characteristic corneal changes, although some were symptom free at the time of the examination. An additional 14 girls who had no complaint referable to their eyes but who worked in the vicinity of the affected girls were examined, and 9 of these employees were found to have the characteristic corneal changes. Five girls from a department not concerned with cementing were also examined, and none was observed to have abnormalities of the cornea.

The fact that the corneal disturbances were noted exclusively in women is probably not significant in view of the preponderance of women employees, but it is noteworthy that the 1 man examined, the chemist's assistant, showed no significant abnormality of his corneas, although he was allegedly exposed to high concentrations of the solvent vapors.

The ages of the women affected ranged from 19 to 63, with a distribution roughly corresponding to the general age distribution of the plant employees.

Symptoms.—Of the 28 workers who were observed to have the corneal changes, only 19 had complained of ocular irritation. The outstanding symptoms were foreign body sensation, epiphora and burning of the eyes. These were

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1. Krüger, E.: Augenerkrankungen bei Verwendung von Nitrolacken in der Strohhutindustrie, Arch. f. Gewerbepath. u. Gewerbehyg. **3**:798, 1932.

2. Tabershaw, I. R.; Fahey, J. P., and Skinner, J. B.: Personal communication to the authors.

3. The butanol concentrations were measured by Mr. J. B. Skinner, according to a technic to be described in the report by Tabershaw, Fahey and Skinner.[2]

characteristically worse, sometimes severe, on the patient's first awakening in the morning or on her awakening at night. The symptoms often disappeared entirely during the day. Less regularly noted were blurring of vision (acuity was reduced to 20/100 in 1 of the most severely affected patients), itching and swelling of the lids. Only occasionally had the patients noted redness of their eyes.

During the period that the patients were under observation the plant closed down for one week. Several of the patients had stated that when they were away from work for the weekend their eyes felt better, and that after they had been back at work for two or three days their eyes again became irritated. The 13 employees who had had the most severe symptoms prior to closure of the plant were therefore reexamined after the week's respite. At this time 10 were symptom free, while 3 continued to have symptoms, with little if any improvement.

Signs.—Of the 35 employees examined from the department engaged in the cementing process, 28 showed characteristic and symmetrically distributed corneal lesions. In patients with the more severe conditions there was a slight haziness of the cornea that could be seen grossly with oblique illumination, but in the majority of patients the lesions could be seen only with slit lamp microscopy. Without exception, the anteriormost portion of the cornea (presumably epithelium) was studded with fine dots, which appeared gray with direct illumination but were seen to be clear vacuoles with transillumination. The vacuoles were limited to the palpebral fissure and were especially numerous in the central portion of the cornea. The vacuoles varied in size, having an average diameter that was estimated to be of the order of magnitude of 0.05 mm. There was no apparent infiltration about the vacuoles and none of the cloudiness of the epithelium associated ordinarily with epithelial edema. The number of vacuoles varied, the patients with the mildest involvement showing not more than 10 to 20 in the whole cornea and the patients with the more severe conditions showing 500 to 1,000. The severity of symptoms usually, but not invariably, corresponded to the number of vacuoles. The surfaces of the corneas were uniformily lustrous and only rarely showed punctate staining with fluorescein. With introduction of granules of sudan IV on the cornea, no red staining of the vacuoles could be demonstrated.

Aside from the vacuoles, the only abnormality that was observed with any frequency was an increased amount of amorphous debris in the precorneal tear film. Corneal sensation was normal in all the subjects tested, and the endothelium showed no abnormality.

After one week's absence from work, 13 patients who had shown numerous vacuoles in the cornea prior to leaving work were again examined. All showed conspicuous objective improvement. Seven no longer presented any vacuoles in the cornea, while the remaining 6 had an average of only 100, in contrast to the former 500 to 1,000. One of these employees who presented pronounced improvement on being away from work for one week was again examined after she had been back at work for four days; she again showed the original involvement, to the extent of approximately 1,000 vacuoles. The same patient was subsequently away from work for ten days because of her ocular symptoms. At the time she left work she had 500 to 1,000 vacuoles in each cornea, with fairly severe symptoms. On the fifth day away from work the number of vacuoles had decreased to from 200 to 500, with persistent, symptoms, although of decreased severity. By the tenth day the signs and symptoms had entirely disappeared. She then returned to work and had a return of symptoms, beginning on the second day and causing her to leave work again on the fourth day. She was, however, not examined at this time until she had been away from work for three days; she then showed moderate involvement of the cornea, with 100 to 200 vacuoles.

The observations indicate that when the patients are away from work, the corneal changes are considerably improved in five to seven days and, even in the most severe condition, may be completely resolved in ten days. With reexposure of the patients, the corneal changes again appear within a few days and may attain the maximum in as short a period as four days. We did not have any information on the length of time a new worker must be exposed before the corneal lesion developed.

In all patients the objective signs were qualitatively similar. The observations on 1 of our patients were, however, especially noteworthy. Together with the usual distribution of vacuoles in the cornea, one eye showed a series of densely packed, fine vacuoles forming a vertical line just to one side of the corneal center. The line was approximately 3 mm. in length and 0.5 mm. in width and was bordered on each side by a translucent edge. There was no opacity. When the patient returned, after absence from work of one week, the translucent zone was still present and unchanged, but the vacuoles had entirely disappeared. This zone is assumed to be the site of a former abrasion, now represented by thick-

ened epithelium, and the condensation of vacuoles within this area is interpreted as being consistent with the previously assumed intraepithelial position of the vacuoles.

Course and Treatment.—The observations already cited indicate the ephemeral nature of the corneal disturbance and its obvious improvement within a few days after removal from exposure. The disorder has not resulted in any serious sequelae in the patients whom we have followed and has necessitated only a minor degree of absenteeism. The treatment of 1 patient with repeated instillations of oil (Mazola was used, in the absence of olive oil) was without effect. The obvious therapy at present is improved ventilation in the industrial plants.

EXPERIMENTAL OBSERVATIONS

Mice, guinea pigs, rabbits and dogs were exposed to the vapor of a mixture of butanol, denatured alcohol and diacetone alcohol, in an attempt to reproduce experimentally the corneal lesions seen in the foregoing series of patients. Examination of the animals, like that of the patients, was made by means of the slit lamp.

Eight mice were exposed continuously to the vapor of a mixture of 90 per cent butanol and 10 per cent diacetone alcohol in lethal concentrations for sixty-eight hours. A fresh vapor-air mixture was passed continuously through the exposure chamber.

Two mice died during the first forty-six hours and were not examined. A third mouse was unconscious at this time but revived on being removed from the exposure chamber. This mouse had swollen, somewhat opaque corneas, loose corneal epithelium and cataracts. The other 5 mice had normal corneas at the end for forty-six hours, and the exposure was continued. Three of these mice were dead by the sixty-eighth hour; the other 2 animals were unconscious. The latter 2 mice had swollen, opaque corneas, loose corneal epithelium and cataracts. None showed the characteristic vacuoles seen clinically in human beings.

Six guinea pigs were exposed to butanol vapor in sublethal concentrations for periods as long as seven days. Again, no characteristic vacuoles in the cornea were noted, although corneal ulcers, attributed to exposure keratitis, did occur when the animals were unconscious.

Three rabbits and 2 guinea pigs were exposed to a lower concentration of butanol vapor, approximately 300 parts per million, continuously for two weeks. One rabbit and 1 guinea pig died during the two weeks, but neither these nor the survivors showed the characteristic vacuoles in the cornea.

Four rabbits and 2 dogs, all having normal eyes, were similarly exposed continuously for two weeks to the vapor of a mixture of 50 per cent butanol, 25 per cent denatured alcohol and 25 per cent diacetone alcohol, at a vapor concentration of approximately 125 parts of butanol per million. All the animals survived, and none of them showed any lesions in the cornea.

To determine what role preexisting lesions of the epithelium might have, the cornea of one eye each of 3 rabbits was completely abraded by being scraped with a knife, and the animals were exposed for two weeks continuously to the vapor mixture of 50 per cent butanol, 25 per cent denatured alcohol and 25 per cent diacetone alcohol, at the same concentration as in the preceding experiment. The abraded corneas did not reepithelize as rapidly as normally. The cornea of one eye of each of 2 rabbits which was similarly abraded but not exposed to the vapors was entirely healed on the second day, whereas the 3 abraded and exposed corneas showed gross defects of the epithelium and swelling and haziness of the stroma on the fourth day. By the tenth day the latter lesions were epithelized, but 2 of these eyes continued to show haziness of the stroma. However, at no time were vacuoles similar to those observed in the patients seen in either the unabraded or the abraded corneas.

COMMENT

The clinical syndrome presented here, the chief feature of which is the presence of vacuoles in the epithelium, is unique, so far as we are aware. The appearance differs from that of epithelial edema in that the corneal surface is smooth and the cornea between the droplets is optically clear. The lesions also differ from Vogt's keratitis epithelialis vesiculosa in the characteristic absence of staining with fluorescein. The droplets which are occasionally seen in association with arcus senilis bear some resemblance to the vacuoles noted in our patients except that droplets occurring with arcus senilis are situated in the stroma and at the periphery of the cornea and do not show variations from day to day. The syndrome bears the most pronounced resemblance to post-traumatic relapsing keratitis. The symptoms are the same, and so are some of the signs, for one occasionally notes translucent droplets in the epithelium in patients with relapsing keratitis at a time when there is no "take" with fluorescein. The syndrome differs from relapsing keratitis in the absence of any history of trauma and the distribution of vacuoles symmetrically in the central area of both corneas.

There can be little doubt from the clinical evidence that the cause of the disease is exposure to butanol. Its outbreak was definitely associated with the use of butanol in this and in other factories. We have, however, been unable to produce the condition in animals with exposures to concentrations greater than those to which the patients were exposed and for periods as long as those which are known to produce an exacerbation in human beings.

SUMMARY

The characteristics of corneal lesions presumably caused by butanol are described for the first time. The characteristic lesions consist of numerous translucent vacuoles situated in the most superficial layers of otherwise normal corneas. The symptoms consist chiefly of pain and epiphora, most severe when the patient first opens the eyes on awakening. Both eyes are affected almost symmetrically. The lesions are related to occupation, being noted only among "raincoat cementers" in the plant studied, and are observed in many employees who have no symptoms. The lesions improve spontaneously within a few days of the patient's being away from work and recur within a few days after return to work.

Clinically, there is little doubt that butanol or some mixture of butanol, diacetone alcohol and denatured alcohol is responsible, since the lesions occurred only when these agents were used, and ocular irritation has been noted in other plants in which butanol was employed. However, exposure of mice, guinea pigs, rabbits and dogs to the vapor of butanol or of mixtures of butanol, diacetone alcohol and denatured alcohol has been uniformly unsuccessful in reproducing the condition seen in human beings.

243 Charles Street.

DIFFUSE NEUROFIBROMATOSIS (VON RECKLINGHAUSEN'S DISEASE) INVOLVING THE BULBAR CONJUNCTIVA

REPORT OF A CASE, WITH LESIONS OF THE SKELETAL SYSTEM AND SKIN, BODILY ASYMMETRY AND INTRACRANIAL INVOLVEMENT

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In 1882 von Recklinghausen first described this disease and named it neurofibromatosis. In 1894 Landowsky noted the fundamental symptoms of the condition, namely, cutaneous pigmentation and tumors of the skin and nerves. Later it was discovered that the skeleton was also involved. Psychic disorders were often noted (Depetris and associates [1]). Later records showed that the neurofibromatosis was associated in some cases with cranial lesions and in others with disturbances of the glands of internal secretion and with ocular disorders or abnormalities of the ocular adnexa. The name was the subject of dispute; thus, fibrogliomatosis and schwannosis were mentioned as appropriate designations (Herrmann and Morel [2]). The familial, hereditary, congenital character of the disease was demonstrated. The condition shows a hereditary disposition or propensity to occur irregularly through several generations. Abortive (incomplete) and monosymptomatic forms have been mentioned.

The condition must not be confused with the other disease described by von Recklinghausen —fibrocystic osteosis, parathyroid osteosis or generalized osteitis fibrosa cystica, with hyperfunction of the parathyroids due to adenoma of these glands. This condition is characterized by an osseous syndrome (osseous cysts, lack of calcium in the bones and osteoclasia) and a humoral syndrome (hypercalcemia, hypercalciuria and hyperphosphaturia, with an increase in the phosphatase content of the blood), but not the cutaneous syndrome characteristic of neurofibromatosis.

According to Pavišič,[3] neurofibromatosis may affect the extradural or peripheral portions of the nerves or their intradural portions, with invasion of the cranial nerves in the actual substance of the brain. Neurofibromatosis universalis, according to the opinions expressed by Orzechowsky and Novicki, is the combination, through the union of affected family lines, of tuberous sclerosis and neurofibromatosis.

Verocay expressed the belief that the disease ought to be called neurinomatosis, to indicate that the tumor derives from rests which do not differ from Schwann cells. Lhermitte designated it neuroglioma, and Masson, schwannoma. Pavišič stated the opinion that the disease is systemic, arising through disturbances in the development of the embryo of the mesodermal and ectodermal layers, and that one may agree with Verocay that it is a true tumor of the nerve fibers, of neurectodermal origin (neurinoma plexiforme), or else arising from growth of the endoneurium and perineurium, with secondary and reactive hypertrophy of the fibrous tissue.

According to Davis,[4] neurofibromatosis of the nerves of the periosteum of the orbit may cause subsequent erosion and invasion of the osseous wall, or there may be erosion or thinning of the bones through the mechanical effect of pressure on the part of the tumor. Three clinical forms of neurofibromatosis may exist: (1) predominant invasion of the central nervous system (intracranial organs); (2) predominant invasion of external structures (skin), and (3) involvement chiefly of the skeletal system.

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Read, with presentation of the patient, at a meeting of the Argentine Society of Ophthalmology, Aug. 18, 1943, Buenos Aires, Argentina.

1. Depetris, P.; Ferraris, A., and Zarázaga, J.: Enfermedad de Recklinghausen en la infancia, Semana méd. **1**:1274-1286 (June 18) 1942.

2. Herrmann, G., and Morel, C.: Tratado de anatomía patológica, Barcelona, 1917, vol. 2, p. 681.

3. Pavišič, Z.: Ueber einen Fall von Neurofibromatose der Lider, Klin. Monatsbl. f. Augenh. **105**:490-495 (Oct.) 1940.

4. Davis, F. A.: Plexiform Neurofibromatosis of the Orbit and Globe, with Associated Glioma of Optic Nerve and Brain: Report of Case, Arch. Ophth. **22**: 761-791 (Nov.) 1939.

OCULAR LESIONS

A review of the literature from 1932 to 1942 revealed that when the ocular apparatus and the ocular adnexa are affected the parts most frequently attacked are, first, the eyelids and the optic nerve, followed by the orbit, the retina, the iris, the cornea, the tarsal conjunctiva and, last, the bulbar conjunctiva.

There may be hyperplasia and thickening of the skin of the eyelids and the neighboring temporal and facial regions; tumors, both large and small, of the eyelids and the superciliary region; palpebral ptosis, as well as pseudoptosis; growths and tumors of the tarsal and, more rarely, of the bulbar conjunctiva; nodules of the cornea; tumors of the iris and disturbances in the pigmentation of the iris; exophthalmos; enophthalmos; thinning of the orbital wall; glaucoma; tumors of the optic nerve and the retina and choroid; ocular pulsations; strabismus; orbital asymmetry; amblyopia, and abnormalities in the size and shape of the orbit.

In view of the frequency with which neurofibromatous tumors are located in the conjunctiva, I shall quote Duke-Elder's [5] statement that "neurofibromatosis of the conjunctiva is extremely rare." He cited von Michel's case of involvement of the bulbar conjunctiva (1908) and Guist's case of lesions of the bulbar and nasal conjunctiva (1920).

In Argentina, Soriano and Picoli [6] and Ibañez Puiggari and Gaviña Alvarado [7] have reported cases of neurofibromatosis with predilection for the eyelids, with invasion of the tarsal conjunctiva. Dimitri, Morea and Just noted neurofibromatosis associated with an intracranial tumor.

In the world literature indexed in the *Quarterly Cumulative Index Medicus* from 1915 to 1942, I found only the article by Loos [8] on neurofibromatosis of the bulbar conjunctiva. Therefore the case reported here is of interest, since it is the fourth instance of neurofibromatosis of the bulbar conjunctiva on record. In the *Quarterly Cumulative Index Medicus* 34 cases of neurofibromatosis with ocular complications, involving the eyelids, the optic nerve, etc., were reported from 1932 to 1942.

PRESENTATION OF CASE

The case I present is interesting because it concerns a neurofibromatous tumor which invaded the bulbar conjunctiva exclusively with confirmation by histopathologic study, and the clinical history, as will be seen later, revealed the following significant features: (1) twinship, (2) coexistence of neurofibromatosis and epilepsy, (3) bodily asymmetry, (4) intracranial disorders, (5) skeletal lesions, (6) cutaneous lesions (tumors), (7) partial alopecia of the scalp on the side of the affected eye and (8) slight mental retardation.

There were faintly outlined café au lait spots at the lumbar level; these spots were not clearly marked because the patient was fair, with very white skin—the kind which, as is well known, does not show pigmentation as clearly as dark skin. I mention the café au lait pigmentations of the skin because they are typical of neurofibromatosis.

There is evidence that the hypophysis is affected in many cases of this disease. An enlarged sella turcica was observed by Vogt [9] and Knapp [10] and in the present case. D'Anostini [11] stated:

> From experimental work and clinical, anatomicopathologic and therapeutic observations it is concluded that the elaboration of pigment depends on two regulating and antagonistic influences: the sympathetic nervous system and the hypophysis. . . . The sympathetic nervous system inhibits formation of pigment; the hypophysis, on the other hand, by means of the melanophore hormone which it secretes, encourages the production of pigment; the absence of this hormone would result in achromia.

Clinical Features.—In the present case, the diameter of the right orbit was greater than that of the left, as was true in the cases described by Davis [4] and Pavišič.[3] In my case, as in a case reported by another author, the disease occurred in a twin. Maygrier and Schwab [12] stated that "one of the twins may be ill shapen and show slight deformities." Recklinghausen's disease and epilepsy were associated in the case studied by Pallasse and Mar-

5. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1938, p. 1790.

6. Soriano, J., and Picoli, H.: Dos casos de enfermedad de Recklinghausen, Arch. de oftal. de Buenos Aires **10**:620-632 (Aug.) 1935.

7. Ibáñez Puiggari, M., and Gaviña Alvarado, E. R.: Una observación interesante de enfermedad de Recklinghausen, recidiva post-operatoria, Semana méd. **1**:1230-1237 (April 13) 1933.

8. Loos, F.: Ueber doppelseitige Neurofibromatosis der Lider, Konjunktiva und Kornea, der Lippen und der Zunge, Klin. Monatsbl. f. Augenh. **89**:184-189 (Aug.) 1932.

9. Vogt, cited by Pavišič.[8]

10. Knapp, A. A.: Case Presenting Involvement of Left Eyelids, J. A. M. A. **100**:494-495 (Feb. 18) 1933.

11. d'Agostino, M.: Sobre las posibles relaciones del vitiligo con las neoplasias viscerales, Semana méd. **2**:134-138 (July 15) 1943.

12. Maygrier, C., and Schwab, A.: Précis d'obstétrique, ed. 2, Paris, G. Doin, 1922, p. 137.

met.[13] Psychosis and neurofibromatosis were present in Haselager's case.[14] Craniofacial asymmetry was also noted in 1 of the cases reported by Garzón and Arguello Pitt.[15] Palpebral ptosis was present in the cases reported by Davis,[4] Pavišič.[3] Soriano and Picoli,[6] Ibañez Puíggari and Gaviña Alvarado[7] and Knapp[10] and in my case. Partial alopecia, similar to that presented by my patient, existed in the case of Touraine and Picquart.[16] An epipapillary membrane, which was present in my case, was noted in the cases of Pavišič[3] and Christi and Naville.[17]

In the case recorded by Davis the orbital nerves, as well as the sclera, choroid, ciliary body and iris, were involved in the neurofibromatosis. There were present in addition glioma of the optic nerve, as well as gliomatosis of the intracranial portion of both optic nerves, the optic chiasm and the thalamus, and a glioma of the temporal lobe of the brain.

The bodily asymmetry, which was present in my case, with the left side less well developed than the right, may be interpreted as a crossed lesion resulting from involvement of the right side of the brain, with trophic disorders, which were partially visible in the roentgenogram.

Clinical History.—C. Z., a girl aged 18, single, was the twin of an apparently healthy boy. Her weight was 58 Kg. Her height was 168 cm. when she stood on her right leg and 167 cm. when she stood on her left leg. The greater length of the right leg was noticeable on account of the bodily asymmetry.

Family History.—Her maternal grandparents were living and apparently healthy. Her paternal grandparents were dead. The grandmother, who died at the age of 42, had "head trouble." A first cousin of the father's and a first cousin of the mother's each had 2 pairs of twins. Two first cousins of the patient's were subject to epileptic fits. Her only brother, except for her twin, died at the age of 2 years, of bronchopneumonia.

Personal History.—The patient was born at term, of a biovular pregnancy; her twin brother is living and well. Her weight at birth was approximately 4,000 Gm. Feeding was artificial after the first month. She had pneumonia at the age of 2 years and measles, pneumonia and scarlet fever during childhood. She had had epileptoid fits from infancy, with only transitory headache after the fits. Menstruation had been irregular; she had a period of amenorrhea for six months, but menstruation had been regular during the seven months prior to examination.

The lesions which she presented were congenital. The tumors of the skin and those of the conjunctiva underwent a slight increase in size, which was very slow and painless, during adolescence.

Present State of the Eyes.—Right Side: The skin and subjacent tissues in the region of the eye manifested hyperplasia. There was cranio-orbital asymmetry, the eye, as well as the eyelids, on this side being placed on a more anterior plane than the corresponding structures on the left side. The skin of the forehead was rough and slightly reddish. Ptosis was present (fig. 1).

A pale pink tumor, the size of a hazelnut, was noted in the superciliary region, with some alopecia of the eyebrow above it; it did not adhere to the deep tissues. A small tumor, the size of a grain of rice, lay on the outside of the middle of the upper eyelid, with two or three hairs on it. This growth was removed for histologic study.

Fig. 1.—Photograph showing the tumor in the superciliary region, as well as the small tumor in the skin of the eyelid and the ptosis of the same lid, all on the right side.

The palpebral portion of the lacrimal gland was somewhat hypertrophied and hyperemic. In the bulbar conjunctiva was a flat, paralimbal tumor, at 3 o'clock. The growth was rounded, with a smooth surface and neat edges. It measured 5 mm. in diameter, was pale pink and did not adhere to the deep tissues. It invaded the cornea 1 mm. in a horizontal and 4 mm. in a vertical direction.

On the outside of the caruncle, a few millimeters from it, was a tiny, elongated, polypoid tumor, which moved with the conjunctiva. This was excised for histologic examination.

The large tumor (fig. 2), from which I took two fragments for pathologic study, occupied almost two thirds of the bulbar conjunctiva above the cornea; it was slightly triangular, with the base directed upward and the vertex truncated; the top of the tumor reached the fornix and the base extended to the limbus, actually invading the cornea for about 1 mm. in a vertical and 6 mm. in a horizontal direction. The tumor measured easily 2 cm. in its widest part and almost touched, on the temporal side, the outer part of the lacrimal gland. The edges, except the upper, were well defined. The growth had an encapsulated appearance. Not a few fine vessels were to be seen on the surface, which was smooth except for a slight globular prominence on its highest portion. The tumor was salmon pink, did not adhere to the sclera, was of soft consistency and caused no pain. The rest of the conjunctiva, especially on the

13. Pallasse, P., and Marmet: Maladie de Recklinghausen et épilepsie, Lyon méd. **156**:618-620 (Nov. 24) 1935.

14. Haselager, P. J.: Symptomatic Psychosis in Recklinghausen's Disease, Nederl. tijdschr. v. geneesk. **79**:4461-4466 (Sept. 21) 1935.

15. Garzón, R., and Arguello Pitt, L.: Recklinghausen's Disease, Rev. argent. de dermatosif. **21**:414, 1937.

16. Touraine, A., and Picquart, A.: Maladie de Recklinghausen a pigmentation systématisée vitiligo, pelade, Bull. Soc. franç. de dermat. et syph. **44**:81-85 (Jan.) 1937.

17. Christi and Naville, cited by Pavišič.[3]

upper and nasal side, was reddish and showed hyperplasia.

A pointed paralimbal spot and a small limbal growth were noted in the upper inner sector of the cornea.

The anterior chamber, the iris, the crystalline lens and the vitreous humor were normal. The pupil reacted normally.

Ocular tension was normal. Motility was normal.

Refraction revealed simple astigmatism, measuring +2 D. cyl., axis 60. Vision was 1/6 without correction. It could not be corrected either with stenopeic hole or with lenses.

Examination of the fundus revealed a very thin prepapillary membrane, which lightly veiled the papilla, and a white foveal halo; the latter was visible because of the sclera and vaguely suggested, on indirect ophthalmoscopic examination, the appearance of the fundus in high myopia.

The reflex was hardly visible. There was scarcity of retinal pigment characteristic of the fundus of a blond person, which allowed good visibility of the choroid vessels. The vessels of the retina, arteries and veins

Fig. 2.—The tumor in the bulbar conjunctiva, above the cornea, is noticeable. Histologic study showed it to be von Recklinghausen's neurofibroma.

were of normal caliber. There were no hemorrhages or white spots.

The color fields were normal. The field of vision, determined with Malbran's perimeter and campimeter, was normal.

Palpation and auscultation of the ocular apparatus on the right, or affected, side revealed no bruit or pulsation.

Left Side: The ocular adnexa, the anterior and posterior segments of the eyeball, the fundus and the field of vision were all normal.

Comment: The disease was unilateral, affecting only the eyeball and the ocular adnexa on the right side.

I removed two fragments of the large tumor on the bulbar conjunctiva situated above the cornea, the small paracaruncular tumor and the small tumor on the outside of the eyelid, all of which were sent to Dr. Juan P. Picena, professor of pathologic anatomy of the Faculty of Medicine in Rosario, Argentina, for histologic examination, a report of which is given later. He made the diagnosis of diffuse neurofibromatosis.

General Clinical Examination (Dr. Armando E. Orellano).—The patient walked with a slight limp. The head was asymmetric, the right temporoparietal region being more prominent than the left. The neck, the organs of circulation and respiration and the abdominal organs, including the liver, spleen and kidneys, showed nothing remarkable.

The arterial blood pressure was 13 cm. maximum and 6 cm. minimum.

The limbs on the left side were less well developed than those on the right.

Examination of the Skin (Prof. Dr. Schujman).—In the temporal and parietal regions on the right side were two large areas of alopecia (fig. 3). In the area in the temporal region the skin was raised at the periphery and was depressed in the center, and in this slight depression could be seen a pale violet tumor, the size of a hazelnut. In the area of alopecia in the parietal region there was an umbilicated scar, the size of a 5 centavo piece. Palpation of these areas of alopecia revealed soft infiltration of the skin and the tumors, especially the latter. There were certain osseous irregularities, especially in the region of the umbilicated

Fig. 3.—One tumor and two zones of alopecia in the temporal and the parietal regions, on the side of the affected eye.

depression. There was no pain. The skin slid over the deep tissues. Pigmentary nevuses were noted over the rest of the skin of the body.

Ear, Nose and Throat (Dr. Gomez Galissier).—Nothing pathologic was observed.

Neurologic Examination (Dr. Luis Bonsembiante).—The patient presented a convulsive syndrome preceded by an aura of tickling in the epigastric region. Tonic contractions, first in hyperflexion and then in hyperextension, were followed by automatic movements with the right arm (rubbing of the right frontoparietal region with the hand) and then by relaxation of the left arm and leg, all of which took five minutes at the most. On regaining consciousness, the patient showed signs of sleepiness; sometimes she had headache, and always she noted transitory functional weakness. This seizure syndrome was of irregular recurrence, the frequency

varying from once in two months to several times in the same day.

The deep reflexes in the lower limbs were lively and equal on the two sides and were normal in the upper limbs. The left limbs showed slightly diminished muscular tone and increased passive motility.

The patient presented retarded psychic development, chiefly due to the domestic situation and home influence (pedagogic retardation).

Laboratory Examination (Dr. Camo and Dr. Rogoff).—Studies of the blood revealed a negative Wassermann reaction and a white cell count of 4,000, with 44 per cent lymphocytes; cholesterol measured 200 mg., calcium 8 mg., sodium (plasma) 280 mg., potassium (plasma) 25 mg., inorganic phosphorus 4 mg. and chlorides (plasma) 270 mg. per hundred cubic centimeters and the phosphatase content was 0.19 Kay unit.

The alkali reserve was 42 per cent.

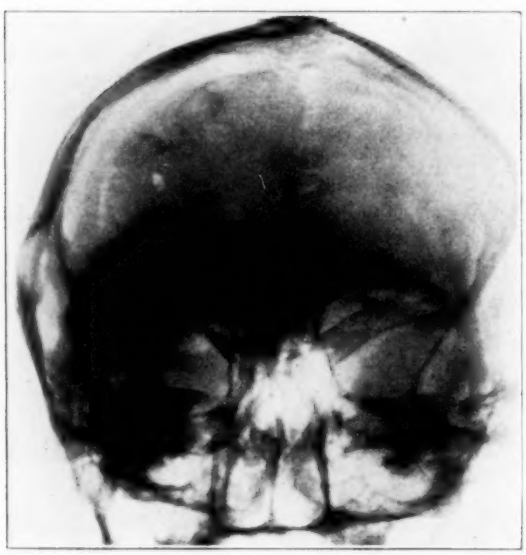

Fig. 4.—The right orbit is larger in diameter than the left. The right temporal region of the cranium protrudes, an aspect of the craniofacial asymmetry. Semicircular shadows appear at the level of the periphery of the right half of the brain.

The phosphates in the urine measured 180 mg. per hundred cubic centimeters.

The Mantoux reaction was negative.

Roentgenographic Report (Dr. Jorge Cenóz).—Cranium and Face: Craniofacial asymmetry was present, owing to protrusion of the region corresponding to the scala of the right temporal bone. The right orbit was larger than the left (fig. 4). The cranium tended to be tower shaped, owing to the greater development of the dome than of the base. The frontoparietal region was thinned, with little difference in the layers of bone, through atrophy of the diploe and accentuation of the inner cortical layer. The middle fossa of the cranium was asymmetric, being deeper on the right side. The deformity was due to internal compression by the right temporal bone.

The sella turcica was larger than usual (fig. 5), especially in the anteroposterior diameter. It was deformed, particularly at the expense of the posterior clinoid processes.

The venous furrows in the right parietal region were accentuated, and "digitate" impressions were present in the left frontoparietotemporal region. On the right side a series of calcium shadows extended from the middle fossa of the cranium to the vertex, some of which were semicircular and gave the impression of being clustered. These calcifications probably circumscribed a series of neurofibromatous endocranial formations.

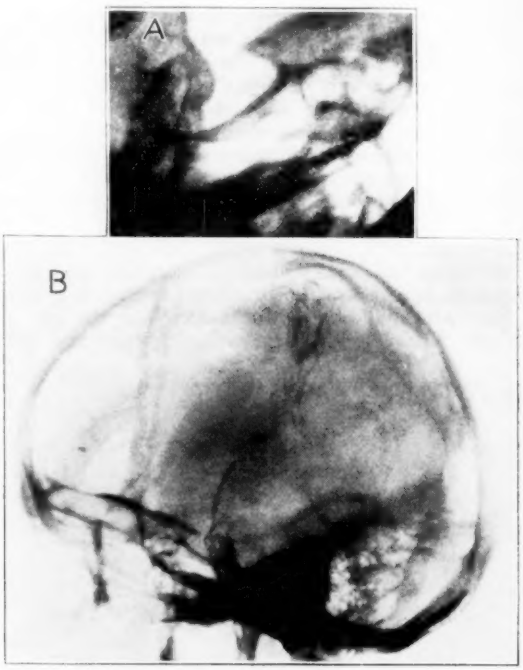

Fig. 5.—*A*, the sella turcica is larger than usual, especially in the anteroposterior diameter. *B*, clumps of shadows extend from the middle fossa of the cranium toward the vertex.

Thorax: No lesions of the bones were visible. The lungs and heart were normal. The dorsolumbar portion of the vertebral column showed no characteristic lesions. The pelvis was moderately asymmetric, owing to the lesser development of the bones which form the left side of the pubis.

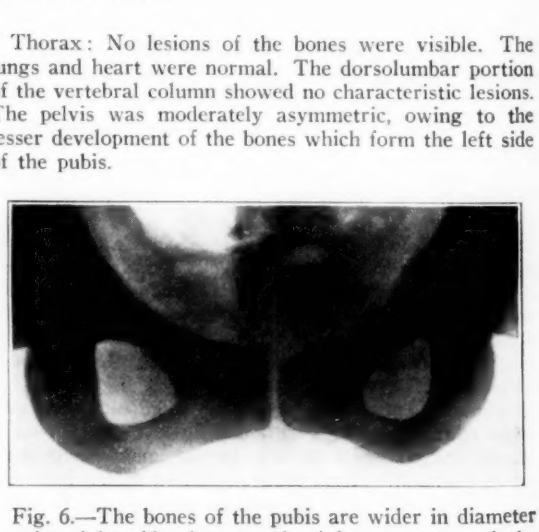

Fig. 6.—The bones of the pubis are wider in diameter on the right side than on the left, an aspect of the bodily asymmetry.

Limbs (fig. 6): The bones of the right arm were more developed than those of the left arm; the left leg was shortened. The inner surface of the upper third of the left tibia presented exostoses.

Cerebrospinal Fluid.—A roentgenogram of the cranium with injection of air into the spinal canal will be

made if necessary. The patient will be referred to the neurologist and to the neurosurgeon for additional study.

Clinical Diagnosis.—The lesions involved the ocular globe; the lacrimal nerve; the external nasal and ciliary nerves, which innervate the bulbar conjunctiva, the eyelid and the superciliary region; the superorbital nerve, and, in the scalp, the superficial branches of the temporal nerve.

Pathologic Study (Dr. Juan P. Picena).—Material for biopsy consisted of tumors of the bulbar conjunctiva of the right eye and a cutaneous tumor from the outside of the upper eyelid on the same side. Three fragments of tissue from the bulbar conjunctiva were received—the smallest, a tiny, round paracaruncular tumor, measuring 4 mm. in diameter, and two larger pieces from the tumor above the cornea, which were soft and together formed a fragment the size of a pea. Another piece, the size of a grain of wheat, taken from the palpebral tumor, was covered with healthy skin, with a small central elevation, also of nonresistant consistency.

Microscopic Study: The small paracaruncular tumor showed simple papillomatous hyperplasia. Entirely different was the histologic appearance of the tumor on the skin of the eyelid and the growth of the bulbar conjunctiva above the cornea, which resembled each other. In the loose cellular tissue appeared two uneven clumps of fibrils, which on superficial examination might be taken for conjunctival elements. Nevertheless, they evidently represented a neuroid formation (Masson) produced through hyperplasia of the schwannian elements, which were often accompanied by Plank-Laidlaw sheaths (fig. 7). The interstitial conjunctival tissue, especially the perineural tissue, clearly participated in the hyperplastic process, which was well demonstrated with the trichromatic aniline blue stain. Not infrequently in some sections the Schwann sheaths appeared thickened and had a central cavity, in which the axis-cylinder was seen. Moreover, in some sections, when a nerve was cut transversely, the axis-cylinder was surrounded by a much more complex sheath, arranged in multiple concentric nucleated layers, an evident hyperplastic phenomenon of the schwannian organ.

Diagnosis.—These lesions were typical examples of the classic neurofibromas of Recklinghausen, which, because of their being diffusely distributed in nerve territory, without being limited to formation of one humor or being restricted to one nerve, should be designated, in accordance with Cid,[18] as diffuse neurofibromatosis.

Fig. 7.—Histopathologic aspect of a section of the tumor of the bulbar conjunctiva, situated above the cornea. Wavy neuroid clumps accompanied by abundant collagen fibers constitute a typical neurofibromatous structure (Dr. Picena).

SUMMARY

C. Z., a twin, had a large tumor of the bulbar conjunctiva, histologic analysis of which revealed a neurofibroma (von Recklinghausen). Moreover, this patient presented asymmetry of the body, cutaneous tumors, partial alopecia of the scalp on the side of the affected eye, skeletal lesions, intracranial involvement and epilepsy. The lesions were congenital.

The tumor is encountered rarely in the bulbar conjunctiva. Duke-Elder [5] cited as the only instances on record the case of von Michel (1908), with involvement of the bulbar conjunctiva, and that of Guist (1920), with lesions of the bulbar and tarsal conjunctiva.

The treatment is extirpation of the tumor and grafting of buccal mucosa to fill the gap that may remain in the conjunctiva.

18. Cid, J. M.: Anatomía patológica de la neurofibromatosis de Recklinghausen, Rev. méd. de Rosario **26**:171 (March); 298 (April); 450 (May) 1936.

ASTIGMATISM AT OBLIQUE AXES AND BINOCULAR STEREOSCOPIC SPATIAL LOCALIZATION

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The means by which one perceives the relative distances of objects in space and their relative orientation constitutes one of the most complex processes of vision. The dioptric images falling on the retinas of the two eyes are essentially flat images, lacking, in themselves, the three dimensional characteristics of the field of the objects observed. Only from the details that make up the pattern of these images on the two retinas can one reconstruct and can one appreciate the depth extent of objects before one's eyes.

According to the current theories of perception, one can attribute the perception of depth, first, to certain psychologic depth motives (*psychische Tiefenmotive*) that arise from particular characteristics of each of the image patterns and, second, to the unique phenomenon of stereopsis that arises from the differences within the two image patterns on the retinas.

The factors designated as psychologic must be considered empiric; that is, the depth relations must have been learned on the basis of experience.[1] These motives may arise primarily from the uniocular image but may, under certain circumstances, also arise from differences in the character of the images in the two eyes.[2] These factors, which include such features as overlay, linear perspective, distinctness of detail and apparent size, are so well known as to require no description here. These clues, or signs, in the images provide the means by which, on the basis of experience, one can interpret from an otherwise flat stimulus pattern on the retina the relative distances of objects from one.

The phenomenon of stereopsis, on the other hand, is generally believed to be a distinct sensation of depth, to be physiologic in nature and based on a phylogenetically acquired organization of the two retinas. It occurs only with simultaneous binocular vision and takes place over the entire binocular field. It can arise only from the disparities of image points within the image patterns of the two eyes. The sensation of stereopsis is distinguished from the psychologic interpretation or concept of depth in that one actually seems to see the empty space between objects in depth.[3]

In normal vision the psychologic depth motives and the process of stereopsis aid, confirm or correct one another in the perception of space. As recently pointed out by Fleischer,[4] they cannot normally conflict in one's familiar surroundings, for both means for space perception are associated with the same depth positions of objects in the field of view.

If the psychologic depth motives are ambiguous, as they may be in certain environments, the stereoscopic sense may provide the basis for the final interpretation of the spatial relationships of objects in those environments. This fact is well illustrated in the experiment with the Ames leaf room,[5] in which the observer holds before one eye a meridional size lens with the axis vertical. The leaf room contains few perspective features which will permit a psychologic interpretation of its shape. On the other hand, stereoscopic vision is stimulated over the whole

From the Research Division of the Dartmouth Eye Institute, Dartmouth Medical School.

1. See, for example, Boring, E. G.: Sensation and Perception in the History of Experimental Psychology, New York, D. Appleton-Century Company, Inc., 1942, chaps. 3, 7 and 8.

2. For example, certain parts of small figures observed at near vision are visible to one eye but not to the other.

3. In papers to be published in the near future, Prof. A. Ames Jr. presents evidence, collected through many years of study of both uniocular and binocular space perception, which substantiates the view that the subjective appearances of objects in space, whether one or both eyes are used, are essentially of the same inherent nature and have the same origin in past experience, both personal and phylogenetic. According to this view, both uniocular and binocular types of depth perception are based on relations to an innately fixed organization in the anatomy of the retinas. Both types are related to psychologic and physiologic processes, and the concept of uniocular space perception as being purely psychologic and of binocular space perception as being purely physiologic is an artificial one.

4. Fleischer, E.: Die Querdisparation als physiologische Grundlage des binokulären Tiefensehens, Ztschr. f. Psychol. **147**:65-132, 1939.

5. A. Ames Jr. will publish a complete exposition of the leaf room and its apparent distortion in the near future. For a brief discussion, see Ogle, K. N.: Association Between Aniseikonia and Anamolous Binocular Space Perception, Arch. Ophth. **30**:54-64 (July) 1943.

binocular field by virtue of the numerous leaves that break up the flat surfaces. The meridional magnifying (size) lens before one eye alters the disparities of the images in the two eyes for all points in the room. The room immediately appears distorted to conform generally to the space figure corresponding to the new image disparity relationships. Moreover, specific details of the room which depend on psychologic depth motives, such as the apparent size of the leaves, also conform to that apparent distortion.

In most normal surroundings, for example, a room with well known objects, such as furniture and windows, in which the perspective and other features can provide dominant psychologic depth motives that are not ambiguous, the changed disparity relationships introduced by the lens generally do not cause an apparent space distortion.[6]

The facts of stereoscopic spatial localization based on the disparities between the images in the two eyes necessitate the hypothesis of corresponding retinal elements as a framework for the specific anatomic organization of the two retinas. Disparate images will be crossed or uncrossed, with the accompanying stereoscopic sensation of being nearer or farther, depending on the relative positions of the images on the retinas of the two eyes within that framework.

The essential problem that arises in this connection is not whether corresponding elements in the two retinas exist, but whether, and to what extent, the retinal organization which they imply is stable. Hering[7] (followed by Hofmann, Hillebrand and Tschermak, as opposed to von Helmholtz, Jaensch and the gestaltists) insisted on the stability and the innate character of this organization. For this discussion it is immaterial whether the sensation of stereopsis arises (1) from specific depth values associated with retinal elements, as conceived by Hering, or (2) from a psychologic process involved in changes of attention, as proposed by Jaensch, or (3) from myosensory influences which occur with the compulsion to fuse disparate images, as suggested, for example, by Fleischer. The fundamental problem remains the same with any of these hypotheses.

The investigations into the problems of aniseikonia and binocular space perception bring new evidence to bear on this question. Among other facts, it has been demonstrated[5] that a correlation exists between aniseikonic errors as measured with the standard eikonometer, which depends on a direct comparison of the image sizes, and the incorrect binocular (stereoscopic) space perception as measured with the Ames space eikonometer.[5] In the latter instrument, all psychologic clues to space localization are eliminated so far as possible, and the subject is forced to use binocular (stereoscopic) vision if he is to localize the relative positions of the test elements. The high correlation found shows that the stereoscopic localization under the test conditions agrees with the type and degree of the difference in size of the ocular images in the two eyes. This occurred despite the fact that the majority of the patients were unaware of any space difficulties in ordinary surroundings. The experiments of Burian[8] on the prolonged wearing of size lenses also bear out these observations and indicate, furthermore, that the image size differences introduced artificially are not compensated for, even though the subject may become adapted in a short time in familiar surroundings to the spatial distortions accompanying those differences.

In line with these results, a study of clinical data suggests that in a large percentage of patients the aniseikonic error measured agrees in type and in approximate amount with what might be expected on the basis of the anisometropia present. Since the implications of such evidence are so far reaching, it is important to make a special study of all aspects of the problem.

In view of the fact, however, that most of the subjects involved in such a study have a spherical anisometropia combined with astigmatic errors, the theoretic image size differences cannot be determined with certainty.[9] Nevertheless, it is possible to study one phase of this problem by considering only cases in which there are astigmatic errors at oblique axes. In these cases one can measure a type of incorrect spatial localization which would be caused by the small rotary deviations of the images in the two eyes, these deviations being associated only with the meridional magnification introduced by the correction of the astigmatism at oblique axes.

6. A. Ames Jr. has already discussed this phenomenon (Aniseikonia: A Factor in the Functioning of Vision, Am. J. Ophth. **18**:1014-1020 [Nov.] 1935).

7. Tschermak, A.: Optischer Raumsinn, in Bethe, A.; von Bergmann, G.; Embden, G., and Ellinger, A.: Handbuch der normalen und pathologischen Physiologie, Berlin, Julius Springer, 1930, vol. 12, pt. 2, pp. 834-1000.

8. Burian, H. M.: Influence of Prolonged Wearing of Meridional Size Lenses on Spatial Localization, Arch. Ophth. **30**:645-666 (Nov.) 1943.

9. This follows in accordance with Knapp's law, which states that in spherical axial (as distinguished from refractive) ametropia, no, or only a small, change in the size of the retinal image occurs with correction. One cannot know a priori what type of spherical ametropia exists in a given case (Ogle, K. N.: Some Aspects of the Eye as an Image Forming Mechanism, J. Optic Soc. America **33**:506-512 [Sept.] 1943).

DECLINATION ERRORS AND ASTIGMATISM AT OBLIQUE AXES

Whenever an ametropia of refractive origin (as distinguished from one of axial origin) is corrected by an ophthalmic lens, a change in the size of the dioptric image on the retina will occur. The optical system, comprised of the ametropic error itself (idealized as an infinitely thin lens at the origin of the error) and the ophthalmic lens in front of the eye, constitutes a telescopic system. There will, therefore, be a magnification (or a diminution) of the image roughly proportional to the product of the ametropic error and the separation of the elements.

The correction of an astigmatic error would result in a meridional magnification (or diminution in the case of a negative cylinder) of the retinal image at right angles to the axis of the correction. Such a meridional magnification distorts the image by elongating it in the meridian of magnification. Associated with this elongation are small rotary displacements of the images

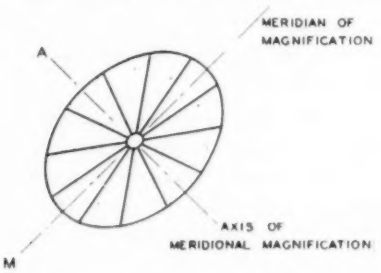

Fig. 1.—Appearance of a wheel with spokes when seen through a meridional magnifier.

of all lines in the object space not parallel with or perpendicular to the meridian of magnification. Thus, the image of a wheel will be elliptic, and the images of the spokes will be displaced toward the meridian of the magnification (fig. 1).

If placed at an oblique axis before one eye, a cylindric lens (or a meridional magnifying lens) will introduce a rotary deviation of the images of all vertical objects in space. When used in connection with the eyes, this particular deviation of vertical objects will be designated a vertical declination error, a name following and extending the terminology introduced by Stevens[10] (fig. 2). These errors, when existing between the images in the two eyes, are of special importance to the problem of aniseikonia, for they cause a particular type of incorrect spatial localization of objects seen stereoscopically in that they appear inclined away from or toward the subject.

10. Stevens, G. T.: A Treatise on the Motor Apparatus of the Eye, Philadelphia, F. A. Davis Company, 1906, p. 235.

The magnitude of the vertical declination error, δ (in degrees), is given with sufficient accuracy by the formula:

$$\delta = 0.20\ m \sin 2\phi, \qquad (1)$$

in which m is the percentage of meridional magnification of the combined lens and eye and δ is the axis of the meridional magnification.[11] Thus, the vertical declination error will be approximately proportional to the meridional magnification and will vary with the axis, being greatest when the axis is 45 or 135 degrees and being zero when the axis is 90 degrees or 180 degrees.[12]

It must be borne in mind that the declination error between the images in the two eyes represents an angular deviation between the images of vertical lines and may have no relationship to the normal declinations of the eyes. The declination error will exist in addition to any changes in the normal declinations as the eyes converge or are raised or lowered.

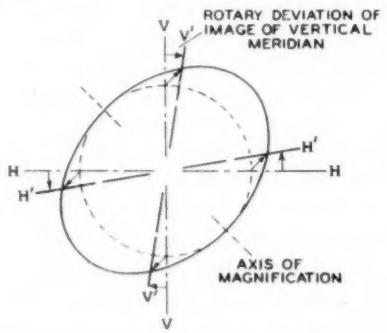

Fig. 2.—Diagram illustrating the vertical and horizontal declination errors introduced by a meridional magnifier at an oblique axis.

The approximate theoretic vertical declination errors, δ, expressed in degrees, introduced by a 1 D. cylindric lens correcting a corneal astigmatism, when placed at various axes, will be as follows:

Axis, Degrees	δ	Axis, Degrees	δ	Axis, Degrees	δ
0 or 180	0.00	60	—0.36	120	+0.36
15	—0.22	75	—0.22	135	+0.43
30	—0.36	90	0.00	150	+0.36
45	—0.43	105	+0.22	165	+0.22

The declination errors for other cylinder powers will be proportional. These values are computed for an ophthalmic lens on a —6 D. base

11. Ogle, K. N.: Meridional Magnifying Lens Systems in the Measurement and Correction of Aniseikonia, J. Optic. Soc. America **34**:302-312 (June) 1944.

12. Attention should be called to the declinations of other meridians and the so-called scissors effect produced by a meridional magnifier. The declination error of the horizontal meridian which will be nearly equal to, but in the direction opposite, that of the vertical declination, has no effect on binocular spatial localization but may conceivably give rise to difficulties in fusion.

curve, placed at a distance of 12 mm. from the pole of the cornea to the center bevel of the lens.

SPATIAL LOCALIZATION AND DECLINATION ERRORS

If a person holds a long thin pencil or knitting needle vertically in his median plane at the level of, and at a distance of about 1 foot (30 cm.) from, the eyes (preferably with a blank wall as background), he can verify, by closing one eye and then the other, that the pencil seen by each eye appears substantially vertical. Now, if the pencil is held inclined, with the top away, he can verify that the pencil seen by the right eye appears slightly rotated in a clockwise direction through a small angle about the visual axis. Seen by the left eye, it appears rotated slightly in the opposite direction, turned counterclockwise (fig. 3).

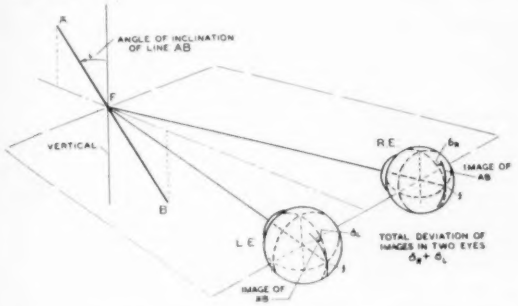

Fig. 3.—Perspective drawing illustrating the rotary deviation of the retinal images of an inclined line in space.

This simple and rough experiment [13] illustrates the relationship that exists between the oblique deviation (rotary displacement) of the images in the two eyes and the corresponding apparent stereoscopic inclination of the object in space. This phenomenon was first demonstrated in 1838 by Wheatstone [14] in his celebrated experiments with the reflecting stereoscope and is well known. The phenomenon results from the stereoscopic depth perception of disparate images.

The relationship between the angle of inclination of the line in space, i (measured from the vertical), and the two angular deviations of the images in the two eyes, measured from the vertical, is expressed with sufficient accuracy by the formula:

$$\tan i = \frac{b}{2a} \tan (\delta_1 + \delta_2),^{15} \qquad (2)$$

in which 2a is the interpupillary distance, b is the visual distance to the fixation point on the line and δ_1 and δ_2 are the angular deviations of the images in the two eyes measured from the vertical meridian.

Conversely, it follows that if an angular deviation were introduced artificially between the images in the two eyes, a given object seen binocularly should, as a result, appear incorrectly inclined and distorted. If placed before one eye at an oblique axis, a cylindric lens or a meridional magnifying lens would introduce just such an angular deviation of the retinal images of vertical objects.[16] In surroundings in which the features providing psychologic depth motives for space perception are dominant this incorrect localization may not occur. In environments in which the psychologic depth motives for space perception are weak the incorrect localization and the accompanying distortion become evident. Furthermore, it is on the basis of this incorrect stereoscopic localization under test conditions that the effective magnitude of the vertical declination error for a given subject can be determined.

The actual magnitudes of the vertical declination errors between the images of the two eyes due to meridional magnifications at oblique axes are small, rarely being greater than 2 degrees and usually less than 1 degree. However, the stereoscopic apparent inclinations of surfaces and their distorted appearance associated with these small errors may be considerable. The apparent incorrect inclinations will be approximately proportional to the visual distance. Table 1 shows

TABLE 1.—*Approximate Theoretic Binocular Stereoscopic Inclination (Degrees) of Surfaces (Measured from the Vertical Meridian) Associated with Given Vertical Declination Errors Between Images in the Two Eyes and for Several Visual Distances*

Total Vertical Declination Error, Degrees	Visual Distances, Degrees			
	6 Meters	3 Meters	1 Meter	50 Cm.
0.10	9	5	2	1
0.25	22	11	4	2
0.50	39	22	8	4
0.75	50	31	11	5
1.00	58	39	15	7
1.50	68	50	22	11
2.00	73	58	28	14

13. Stevens,[10] p. 148.

14. Wheatstone, C.: Contributions to the Physiology of Vision, Phil. Tr., 1838, pp. 371-394.

15. The basis for this formula may be found in Helmholtz, H.: Helmholtz's Treatise on Physiological Optics, translated by J. P. C. Southall, Rochester, N. Y., The Optical Society of America, 1924, vol. 3, p. 349.

16. H. Culbertson (Binocular Astigmatism J. A. M. A. **11**:622-625 [Nov. 3] 1888; Am. J. Ophth. **5**:117-123, 1888) and J. A. Lippincott (On the Binocular Metamorphopsia Due to Correcting Glasses, Arch. Ophth. **18**:18-30, 1889) first described this incorrect localization of space. A more complete description of the distortion of space due to lenses will be made by Ames.

the theoretic inclinations (calculated by formula 2) to be expected for several visual distances and for various vertical declination errors.

Under laboratory conditions the quantitative relationship between the apparent stereoscopic inclination of objects associated with the rotary deviation between the images in the two eyes agrees well with the theory. This is shown, for example, in the data[17] presented graphically in figure 4. The data are the angles of inclination at which a wooden doweling, seen through the half-silvered mirrors of an x-ray reflecting stereoscope, had to be set by an observer in order for its inclination to agree with the apparent stereoscopic inclination from identical x-ray films on each side target when those targets were rotated about the axis of the instrument and set for small angular deviations. The theoretic curves are ours.

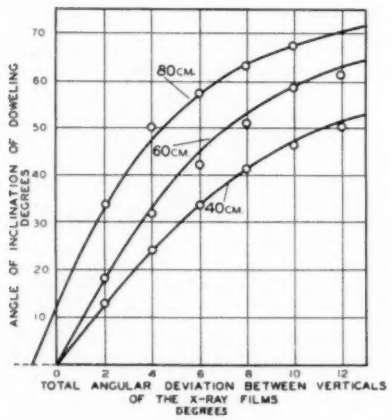

Fig. 4.—Comparison of experimental data and theoretic curves for the apparent inclination of figures observed in an x-ray stereoscope when declinations are introduced between the two eyes. The experimental data were obtained from Meservey.[17]

When unequal astigmatic errors in the two eyes are corrected with ophthalmic lenses, the sizes of the dioptric images in the two eyes will have been magnified (or diminished in the case of negative cylinders). If the axes of the corrections are oblique, a declination error between the images in the two eyes would be expected as a part of the image size differences. A basis for an incorrect stereoscopic inclination of objects in space would then exist.[18] Whether or not the actual aniseikonic condition in a given case will conform to the condition to be expected on the basis of the optical system will depend on a number of factors, the existence of which is at the heart of this discussion.

DETERMINATION OF THE DECLINATION ERROR BETWEEN THE TWO EYES

Measurement of the declination error between the two eyes by means of the incorrect stereoscopic localization presents a number of problems, but it is believed that these difficulties to a large extent have been solved by the invention of the space eikonometer.

In this instrument (fig. 5) an oblique cross, consisting of smooth red cotton cord, is stretched between the corners of a 5 foot (152 cm.) square frame and set up vertically at a distance of 3 meters from the eyes of a subject. The plane of the cross is erected at right angles to, and centered with respect to, the median and the horizontal plane of the subject. Sixty centimeters in front of and 60 cm. behind the oblique cross are hung two plumb lines consisting of smooth green cotton cord, separated 50 cm., which are also centered with and at right angles to the median and the horizontal plane. Also, a vertical plumb line of white cord is suspended so as to pass through the center and lie in the plane of the cross. The test elements are illuminated by several Lumiline lamps, hidden from the subject and mounted so that no shadows will be cast by the elements. The elements are seen against a uniformly black background of cloth. The head of the subject is supported in a suitable head rest, and suitable apertures restrict his binocular field of view wholly to the test elements and also prevent the ends of the cords from being seen.

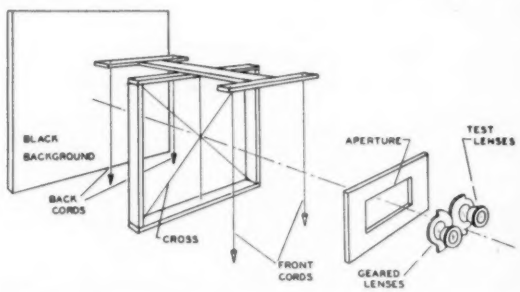

Fig. 5.—Perspective drawing of the space eikonometer as used for measuring vertical declination errors between images of the two eyes.

The general technic for use of the space eikonometer in measuring aniseikonic errors on the basis of binocular stereoscopic space per-

17. These data were taken from the article by Meservey (Depth Effects in Roentgenograms, Am. J. Roentgenol. **39**:439-449 [March] 1938).

18. If the declination error between the two eyes can be determined in addition to the image size differences in the horizontal and vertical meridians, the complete aniseikonic error involving a meridional correction at oblique axes can be calculated. Aniseikonic prescriptions based on this procedure are discussed in the paper by H. M. Burian and K. N. Ogle (Meridional Aniseikonia at Oblique Axes, Arch. Ophth., to be published).

ception is described elsewhere.[19] Here, we are concerned only with the apparent inclination of the test elements when declination errors between the images of the two eyes exist or are introduced by lenses.

The vertical declination error between the images of the two eyes, on the basis of the theory outlined, should cause all the vertical cords to appear inclined fore and aft in space.[20] Moreover, on the basis of the geometric principles of the problem, a meridional magnifier placed before one eye (or both eyes) at an oblique axis can cause the plane of the cross to appear as though rotated about a vertical axis only. Actually, however, all but a few subjects see the plane of the cross inclined, while the cords appear to remain vertical. The nature of this inversion need not be discussed here. Experimental study shows that it does not alter the magnitude of the relative inclination of the cross to the cords. The phenomenon itself may be related to the effect of binocular depth contrast described by Werner.[21]

The relative apparent inclination of the cross to the central vertical cord provides the means of measuring the existing vertical declination error between the images of the two eyes.[22] The measurement consists in introducing an opposite declination error between the eyes to offset the existing error, and thus to cause the cross and the central cord through the cross to appear to lie in the same plane. The device for accomplishing this (fig. 6) consists of a pair of matched 2 per cent meridional size lenses, one before each eye, mounted in rings that are geared together so that they can rotate equally but in opposite directions. The two lenses can be rotated by a suitable handle or knurled drum, the degree of rotation being indicated on an attached scale. When the axes of the two lenses are parallel (and vertical), their effect is zero so far as differences in the sizes of the images in the two eyes and their effect on binocular vision are concerned. If the two lenses are rotated through a small angle, ρ, so that the axes of the two lenses converge upward (positive) or downward (negative), a change in vertical declination is introduced between the images in the two eyes, without a change in the horizontal or the vertical image sizes being effected.

The relationship between the angle of rotation, ρ, of the lenses and the corresponding vertical declination error, δ (expressed in degrees), between the two eyes is given by the formula

$$\delta = 1.12 \sin 2\rho.$$[12]

The scale on the device is calibrated to read the value for δ directly in tenths of degrees. Obviously, the scale is not linear with respect to ρ. Rotation of the lenses so that their axes converge upward causes the plane of the cross to appear inclined, with the top nearer the subject.

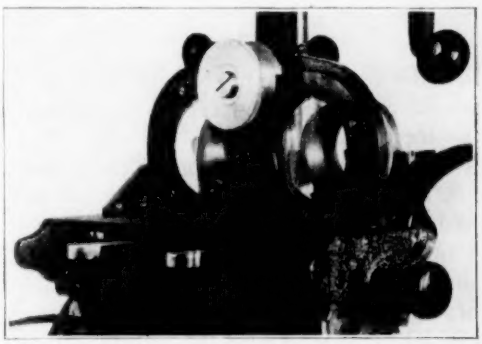

Fig. 6.—Optical device used before the eyes in the space eikonometer to measure the vertical declination error between images in the eyes.

In a given test, the data for the correction of the declination error between the images of the two eyes are obtained by questioning the subject as to the apparent inclination of the cross, as the examiner makes different adjustments of the geared lenses. The limits are determined within which the cross and the central cord appear to lie in the same plane, and the midpoint is taken as the measure. The estimate of the sensitivity of the subject to changes in declination is taken as one-half the range between the limits.

PROJECT

It was possible to set up a project in the clinical division of the Dartmouth Eye Institute whereby a study of the declination errors between the images of the two eyes could be made on several hundred clinical subjects. Emphasis was placed on testing those subjects whose refractive corrections included astigmatic errors at oblique axes. These measurements were, of course, only a part of the complete test made

19. Footnotes 5 and 18.

20. In the case of a true cyclotorsion of the image in one eye (in contrast to a vertical declination due to a meridional size lens at an oblique axis), both the cross and the vertical lines should appear inclined, but the inclination should differ in amount (Ogle, K. N.: Theory of the Space Eikonometer, to be published).

21. Werner, H.: Binocular Depth Contrast and the Conditions of the Binocular Field, Am. J. Psychol. **51**: 489-497, 1938.

22. A single vertical cord does not provide an accurate test for determining the presence of declination errors. Subjects are usually insensitive to changes introduced in the declination when such a test object is used, though their sensitivities generally improve when there are other spatial clues in the surroundings, and even with movements of the eyes. Then, however, the nature of the declination errors is not usually disclosed. Only under special test conditions, of which the space eikonometer is an example, can such errors be detected.

with the space eikonometer to determine the general aniseikonic correction.[18] However, the results necessitate a separate report.

The patients were tested only after their refractive errors had been carefully corrected either with new lenses, or with their own if no change was necessary. In the majority of cases the spectacles worn by the patient in the test were standard Tillyer lenses. These particular lenses were used because their relative magnifications are readily available in prepared tables. The distance of the eye wires from the corneas of the eyes was measured. In order to study the part of the astigmatic corrections that could be accounted for by the curvatures of the corneas, keratometric measurements were also recorded.

The ages of the patients ranged from 17 to 70 years, the average age being about 40 years. A record was made of the age at which spectacles were first worn, the length of time they had been worn prior to the examination and how constantly they had been worn.

The subjects tested in the project obviously did not represent a cross section of the general population. Except for the "normal" persons, the majority were subjects who came to the clinic because of ocular symptoms. Nevertheless, it is believed that the results obtained in this study are typical of the general population wearing corrective lenses.

RESULTS

In order to evaluate the results of the measurements of the declination errors for clinical subjects, the results for persons with "normal" eyes must be known. The precision of measurements and of their repeatability must also be known.

A total of 419 subjects were tested. Of these, 30 had "normal" eyes; 80 had no astigmatic errors or had astigmatic errors which were within 10 degrees of axis 90 or axis 180 or had errors which were parallel and equal in amount in the two eyes, and 309 subjects definitely had astigmatic corrections, the axes of which were oblique, that is, deviating from the horizontal or the vertical axis by 10 degrees or more.

Incidence.—The incidence of declination errors between the images of the two eyes for each of the three groups of subjects is illustrated graphically in figure 7. The curves indicate the percentage of subjects whose measured declination error between the images of the eyes was equal to or less than any specified amount. Thus, for measurable declination errors of 0.20 degree or less, there were 97 per cent of the normal group, 80 per cent of clinical subjects with astigmatism of the "nonoblique" type and 54 per cent of the subjects with astigmatism in oblique axes.

The 30 subjects considered as having normal eyes had small or no refractive errors, did not wear and had not worn glasses, had a visual acuity in each eye of 20/20 or better (Snellen notation), had heterophorias within the normal limits and, moreover, complained of no ocular symptoms. Twelve of these subjects were college students, 8 of whom were better than average athletes. The remaining subjects regarded as having normal eyes included professional men, housewives, secretaries, a Maine guide and an aviator. For this group the average of the declination errors between the images of the two eyes was essentially zero, with an average sensitivity to changes in the declination of the order of ± 0.10 degree. Thus, 90 per cent of these subjects had a declination error between the images of the eyes equal to or less than the average sensitivity of the group.

A generally higher incidence of declination errors was found among the 80 subjects with "nonoblique" astigmatism, though even here 50 per cent of these patients had no measurable error.

The 309 subjects with astigmatism at oblique axes showed, unmistakably, a much higher incidence of declination errors, scarcely 10 per cent having no measurable error.

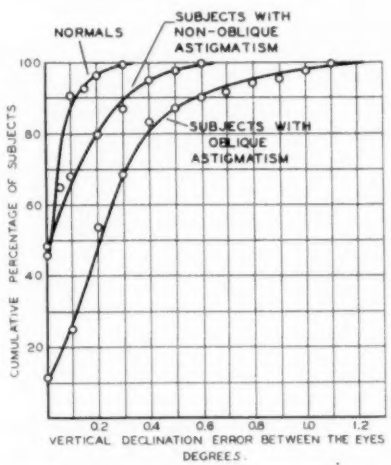

Fig. 7.—Cumulative distribution curves showing the percentage of subjects for whom the measured declination errors lie below given amounts. The curves illustrate the differences found for normal subjects, clinical patients without astigmatic errors or with astigmatic errors the axes of which were not oblique and patients with astigmatism at oblique axes. The sign of the error was neglected here.

Sensitivity.—The sensitivity of clinical subjects in recognizing changes in the declination between the images of the two eyes through the incorrect localization of the cross of the space eikonometer can be found (1) from the limits within which the cross appears oriented correctly, the sensitivity being written as one-half that range, and (2) by having the subject himself adjust the rotation of the geared lenses so that the cross appears oriented correctly, and then determining the mean variation of the settings. With clinical subjects the first method had to be used, and with most subjects the

values determined represented only an estimate of the sensitivity. With trained observers the second method can be used.

For the group of subjects considered to have normal eyes, the average sensitivity, by the method of limits, was ± 0.10 degree. The approximate cumulative distribution of the sensitivities for the normal group is shown in figure 8. In terms of stereoscopic acuity, the high sensitivity of ± 0.10 degree would correspond to about 35 seconds of arc between the retinal images of the two eyes at an angular distance of 5 degrees above or below the visual plane. At a visual distance of 3 meters, 0.10 degree would correspond to an apparent inclination of the cross of the space eikonometer of about 5 degrees.

In a group of 300 men of military age whose ocular characteristics were only a little less normal than those of the 30 subjects previously

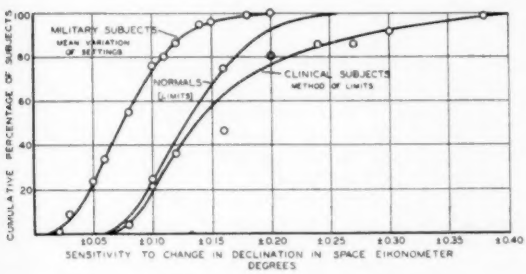

Fig. 8.—Cumulative distribution of different groups of subjects for various sensitivities to changes in declination of images of the two eyes in the space eikonometer test.

described, a study was made of the variability of the subjects' settings of the geared lenses for which the cross of the space eikonometer appeared orientated correctly.[23] The cumulative distribution of the mean deviations from the median of five settings for the group is also shown in figure 8. It will be noted that the sensitivity expressed by the method of limits is of the order of twice the sensitivity when expressed as the mean variation of settings of the geared lenses.

The cumulative distribution curve for the clinical subjects is also shown in figure 8. It will be noted that the sensitivity in this group is only slightly poorer than that of the normal subjects, except for large declinations. Nevertheless, the sensitivities found indicate the general precision of the measurements or declination errors encountered in this study.

23. This study was made by Dr. Henry A. Imus, of the staff of the Dartmouth Eye Institute. A full report will be made on this work.

Repeatability of Measurements.—The reliability of the measurements of the declination error between the images of the two eyes will be indicated by how well the data repeat after a lapse of time. It was difficult to make a statistical study of repeatability on our clinical subjects because the time which elapsed between tests varied so greatly. There is always the possibility that changes in the refractive correction have occurred if the time between tests is long.

Several trained subjects with fairly normal eyes found a maximum day to day variation of the order of ± 0.15 degree, while the average variation from the mean for the measurements over the period was about ± 0.05 degree.

Typical repeatability data on clinical subjects are given in table 2. On the whole, it can be said that the measurements repeat well.

Correlation Between Measured Vertical Declination Error Between the Two Eyes and the Declination Error Calculated from the Astigmatism at Oblique Axes.—A detailed study of the subjects with astigmatism at oblique axes shows that the direction and the degree of the declination errors measured are, in a majority of subjects, related to the existing astigmatism.

The declination error to be expected on the basis of the magnification associated with the corrected astigmatism can be simply computed if one knows the dimensions of the refractive lenses used in the correction and the distances of the lenses from the eyes and has information as to the origin of the astigmatic error. The corneal curvatures can be measured by the keratometer. That part of the subjective astigmatism which cannot be accounted for by the corneal astigmatism must be assumed to be lenticular in origin and will be located at an average distance of 5.3 mm. (reduced distance) behind the cornea (fig. 9). If the subjective and the corneal astigmatism have the same axes, the percentage of meridional magnification (or diminution), m%, can be found with sufficient accuracy from the formula

$$m\% = (\Delta D_1)t/15.23 + Ah + 0.53[A(1 - Ah/100) - C], \quad (4)$$

in which ΔD_1 is the dioptric difference between the curvatures of the front, toric surface of the lens; t is the thickness of the lens, in millimeters; A is the prescribed correction for the astigmatism, in diopters; h is the distance from the vertex of the lens to the pole of the cornea, in centimeters, and C is the corneal astigmatism in diopters. If the toric surface of the lens is the front surface, ΔD_1 will be equal to A. The quantity (1 — Ah/100) corrects for the effectivity of the lens as compared with that of the cornea. The axis of the meridional magni-

fication will be the same as the axis of the astigmatic correction written as plus cylinders. The declination error, δ, can then be found from equation 1.

If the axes of the corneal and the subjective astigmatism differ considerably, it is best to compute the magnifications of two separate systems: (1) the system comprised of the correcting ophthalmic lens and the crystalline lens of the eye and (2) the system comprised of the cornea and crystalline lens of the eye. Then,

$$\left.\begin{aligned} m_1\% &= \Delta D_1 t/15.23 + A(h + 0.53), \text{ and} \\ m_2\% &= -0.53C \end{aligned}\right\} \quad (5)$$

The declination error will be the sum of the errors for each of these magnifications.

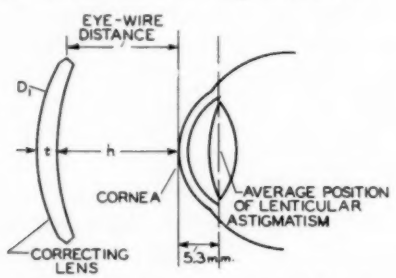

Fig. 9.—Dimensions used in determining the meridional magnification due to a corrected astigmatism.

The total declination error between the eyes will be the sum of the errors in each eye. This value, δ_c, represents the declination error between the images of the two eyes to be expected on the basis of the dioptric meridional magnifications introduced by the corrected astigmatism of the eyes. Table 3 presents the data in several typical cases encountered in the project. The theoretic declination errors between the images of the two eyes, δ_c, were calculated for all the subjects.

A visual method of studying the possible relationship between the measured errors, δ_m, and the calculated errors, δ_c, is to plot the data on a so-called scatter chart. Figure 10 shows the chart for the 309 subjects. Even a cursory inspection of this chart shows unmistakably a positive correlation in spite of the amount of scattering of the points. The majority of the points fall in the upper right and lower left quadrants of the graph, this distribution indicating that the direction of measured error is the same as that of the calculated error.

TABLE 2.—*Repeatability Measurements of the Declination Error on Clinical Subjects*

Case No.	Date of Examination	Refractive Correction	Declination Error, Degrees: Measured, with Variation	Declination Error, Degrees: Calculated
1	10/16/41	R +1.00 D. sph. ( ) −5.00 D. cyl., ax 70 L +1.00 D. sph.	+0.40 ±0.20	+1.10
	9/11/42	R +1.00 D. sph. (X) −5.00 D. cyl., ax 72 L +1.50 D. sph. (X) −0.50 D. cyl., ax 80	+0.55 ±0.20	+0.95
2	10/18/41	R +1.75 D. sph. (X) −1.75 D. cyl., ax 150 L +1.25 D. sph. (X) −1.00 D. cyl., ax 30	−0.30 ±0.20	−1.20
	11/22/41	R +1.75 D. sph. (X) −1.75 D. cyl., ax 150 L +1.25 D. sph. (X) −1.00 D. cyl., ax 30	−0.40 ±0.20	
	4/13/44	R +1.50 D. sph. (X) −2.00 D. cyl., ax 155 L +0.75 D. sph. (X) −1.00 D. cyl., ax 20	−0.55 ±0.15	−1.15
3	1/ 8/42	R +2.00 D. sph. (X) −3.00 D. cyl., ax 100 L +3.25 D. sph. (X) −2.50 D. cyl., ax 85	−0.70 ±0.50	−0.65
	5/ 6/42	R +2.00 D. sph. (X) −3.50 D. cyl., ax 100 L +3.25 D. sph. (X) −2.50 D. cyl., ax 85	−1.00 ±0.25	−0.70
4	2/26/42	R −4.25 D. sph. (X) −0.50 D. cyl., ax 15 L +2.00 D. sph. (X) −7.00 D. cyl., ax 100	+0.55 ±0.55	+1.15
	3/12/43	R −4.25 D. sph. (X) −0.50 D. cyl., ax 15 L +2.00 D. sph. (X) −7.00 D. cyl., ax 100	+0.75 ±0.20	
5	3/28/42	R +1.00 D. sph. (X) −0.75 D. cyl., ax 150 L +1.37 D. sph. (X) −0.75 D. cyl., ax 30	−0.40 ±0.20	−0.65
	8/ 8/42	R +1.25 D. sph. ( ) −1.00 D. cyl., ax 140 L +1.00 D. sph. ( ) −0.75 D. cyl., ax 40	−0.55 ±0.20	−0.85

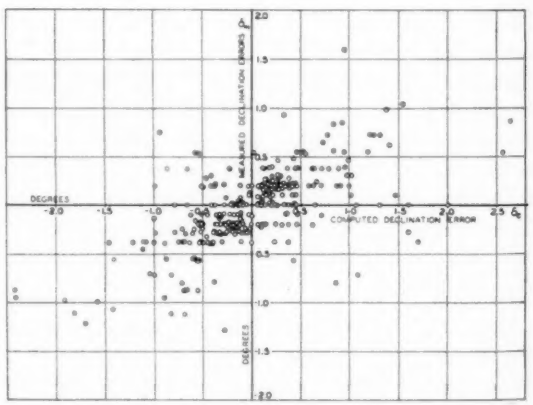

Fig. 10.—Scatter chart of the measured and the computed declination errors, showing a correlation between the two values.

An analysis of the data may be summarized as follows: [24]

	No. of Subjects
δ_m and δ_c in the same direction	225 or 74%
δ_m and δ_c in the opposite direction	44, or 14%
δ_m equals zero, irrespective of δ_c	36, or 12%
δ_m greater than δ_c	45, or 15%
δ_m equal to δ_c	45, or 15%
δ_m less than δ_c	135, or 44%

The important fact in this study is that for 74 per cent of the subjects the measured declination error between the two eyes was in the same direction as that expected on the basis of the magnification of the dioptric error computed by the astigmatic corrections. Moreover, the statistical analysis indicates a significant correlation between the two quantities.

TABLE 3.—*Calculated and Measured Declination Errors Between Images of the Two Eyes of Subjects with Astigmatism at Oblique Axes*

Case No.	Age	Refractive Correction	Keratometric Measurement	Declination Error Between the Two Eyes, Degrees: Calculated	Declination Error Between the Two Eyes, Degrees: Measured
1	30	R −0.75 D. sph. ⊃ −1.25 D. cyl., ax 155 L +0.75 D. sph. ⊃ −1.00 D. cyl., ax 177	−1.12 D. cyl., ax 155 −1.12 D. cyl., ax 180	−0.40	−0.30 ± 0.20
2	44	R +0.62 D. sph. L +0.75 D. sph. ⊃ −0.50 D. cyl., ax 40	−0.75 D. cyl., ax 180 −1.00 D. cyl., ax 180	−0.20	−0.20 ± 0.20
3	34	R +2.25 D. sph. ⊃ −1.50 D. cyl., ax 40 L +2.00 D. sph. ⊃ −1.50 D. cyl., ax 145	−1.25 D. cyl., ax 30 −1.75 D. cyl., ax 150	+0.95	+0.40 ± 0.20
4	33	R Plano ⊃ −0.75 D. cyl., ax 60 L Plano ⊃ −1.50 D. cyl., ax 155	−1.00 D. cyl. ax 25 −2.00 D. cyl., ax 155	+0.55	+0.55 ± 0.15
5	30	R +2.50 D. sph. ⊃ −3.25 D. cyl., ax 15 L +2.75 D. sph. ⊃ −3.50 D. cyl., ax 140	−3.37 D. cyl., ax 15 −3.50 D. cyl., ax 150	+1.40	+1.00 ± 0.20
6	25	R −1.00 D. sph. ⊃ −3.50 D. cyl., ax 170 L −1.00 D. sph. ⊃ −4.00 D. cyl., ax 17	−3.25 D. cyl., ax 170 −3.50 D. cyl., ax 3	−1.45	−0.50 ± 0.10
7	23	R +1.25 D. sph. ⊃ −0.50 D. cyl., ax 170 L +3.25 D. sph. ⊃ −5.00 D. cyl., ax 25 *	−1.50 D. cyl., ax 172 −6.50 D. cyl., ax 19	−1.60	−1.00 ± 0.30
8	48	R +1.00 D. sph. ⊃ −1.00 D. cyl., ax 180 L +5.00 D. sph. ⊃ −5.00 D. cyl., ax 42	−1.25 D. cyl., ax 180 −5.00 D. cyl., ax 42	−1.80	−1.10 ± 0.30
9	62	R −0.50 D. sph. ⊃ −1.25 D. cyl., ax 70 L −4.50 D. sph. ⊃ −1.50 D. cyl., ax 115	−1.00 D. cyl., ax 45 −0.75 D. cyl., ax 150	+0.80	+0.95 ± 0.25

* This astigmatism resulted from corneal ulcers, following an illness at the age of 5 years.

COMMENT

Once a correlation between the measured declination errors between the images of the eyes and the declination errors computed on the basis of the corrected astigmatism is established, the question arises why the two values do not agree in all cases.

To what extent they do not agree can be visualized by studying the distribution of the ratios of the measured to the computed values. This ratio (δ_m/δ_c) is unity if the two values are equal, greater than unity if δ_m is the larger value and less than unity if δ_m is the smaller value. This distribution is shown in figure 11 for the subjects for whom both the measured and the calculated values were in the same and in the opposite direction. As might be anticipated from the scatter chart, the measured value, δ_m, is about 0.6 of the calculated value for the greater number of subjects.

Surprising are the facts that for 14 per cent of the subjects the measured and the calculated declination errors were in opposite directions and that for 15 per cent of the subjects the measured value was greater than the computed value. There are two possible explanations for these facts: 1. In these subjects there may be a basic (not optical) meridional aniseikonic error, such as an anomalous disposition of the retinal elements, which may be greater than, or in a direction opposite, that which was introduced by the corrected astigmatism. That this is a possibility is suggested by the fact that occasionally emmetropes or near emmetropes are found with significant aniseikonic errors. Also, it will be recalled from figure 7 that for a small percentage of subjects with nonoblique astigmatism, significant

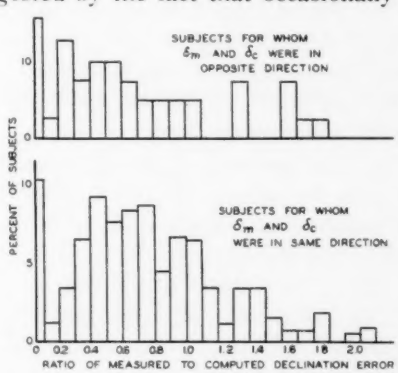
SUBJECTS FOR WHOM
δ_m AND δ_c WERE IN
OPPOSITE DIRECTION
SUBJECTS FOR WHOM
δ_m AND δ_c
WERE IN SAME DIRECTION
PERCENT OF SUBJECTS
0 02 04 06 08 10 12 14 16 18 20
RATIO OF MEASURED TO COMPUTED DECLINATION ERROR

Fig. 11.—A histogram distribution of the ratios of the measured to the calculated declination errors.

24. A statistical treatment of the data gives a Pearson correlation coefficient (r) of 0.64, with a probable error of 0.05. The standard error of estimate was ± 0.26 degree. For 300 subjects this represents a significant correlation. There is no evidence from the diagram that this correlation may not be linear.

declination errors were measured. 2. In these subjects there may be an anomalous cyclic incongruity, or cyclophoria. It is known, of course, that a cyclotropia can also produce an apparently incorrect inclination of surfaces, and this would cause an apparent tipping of the cross in the space eikonometer. A possible cyclotropia is believed to be a real factor. Other suitable instrumentation for measuring and checking this small degree of cyclotropia is not yet available, and additional research is necessary. The fact that the percentage of cases in the two groups is nearly the same suggests that a factor independent of the astigmatism enters into the measurements.

The fact that the measured declination error, δ_m, in a majority of the subjects is less than the calculated declination error, δ_c, might be expected from the usual point of view of physiologic adaptation. However, for only a relatively small proportion, 12 per cent, of the subjects did the declination error between the eyes actually measure zero when the calculated values were not zero.

It might be suggested that the space eikonometer, in spite of the care taken to eliminate empiric visual localization factors, may fail to measure the full declination error present. However, patients who have been given suitable aniseikonic corrections invariably measure no declination error after a lapse of time. If an additional declination error were present, it should appear under these circumstances.

One must allow, moreover, for the existence of a mechanism in the binocular processes which, within certain limits, can actually compensate for image size differences. That this might be possible is suggested by the experiments of Burian [8] on the prolonged wearing of size lenses, for he found that a partial compensation of from one fourth to one third of the image size differences was artificially introduced by the size lenses after about three weeks.

On the 226 subjects with astigmatism at oblique axes for whom δ_m and δ_c were in the same direction, a statistical study was made of the possible relation between the ratio $\delta_m : \delta_c$ and (1) the age of the subject at the time of examination, (2) the length of time spectacles had been worn and (3) the age at which spectacles were first worn.

No relation was found between the ratio and the age of the subject at the time of examination or the length of time that spectacles had been worn. There was, perhaps, a possible relation between the ratio $\delta_m : \delta_c$ and the age at which glasses were first worn; the earlier they were worn, the smaller the ratio tended to be.[25] The latter relation suggests that such a compensatory mechanism is more active in early youth than later in life. However, it must be emphasized that this mechanism, whatever its nature, in the majority of cases fails to correct fully for the aniseikonic error introduced by the astigmatism. Since no association could be found between the magnitude of the ratio of $\delta_m : \delta_c$ and the magnitude of δ_c, which is a measure of the amount of oblique astigmatism present, this mechanism cannot have a constant range but would appear to be proportional to the expected aniseikonic error.

When relatively small uncorrected refractive ametropias exist, the sizes of the retinal images determined by the center of the blur circles are substantially the same as though the refractive errors did not exist.[26] Thus, from an empiristic point of view the more or less fixed relationship between retinal elements in the two eyes might conceivably have developed though the images were slightly blurred. However, measurements were made on subjects whose astigmatism must have been present at birth and was too high to permit any recognition of detail. The measurements on these subjects showed a large declination error between the eyes in the direction indicated by the oblique astigmatism (subjects 7, 8 and 9, table 3).

For several subjects for whom the astigmatism at oblique axes was large and a large declination error was calculated, the measured error was found to be zero. It is possible that a new or anomalous retinal organization for stereoscopically vertical meridians had developed. Such a possibility has already been postulated, for example, by Sachs and Meller [27] to explain the results for a subject who had an unusually high declination but who under normal conditions had no incorrect spatial distortion.

The important inference to be drawn from this study and the correlation found must be that the anatomic and physiologic organization of the two retinas in the binocular processes of vision, for a majority of subjects, must have

25. A simple tetrachoric correlation procedure was used. The age at which glasses were first worn was obtained by questioning the subject, and the answer was often only a guess. Moreover, the nature of the refractive correction worn then was unknown. Only in the case of high astigmatism is there a probability that astigmatic corrections were prescribed at that time.

26. Calculations from the schematic eye show that the change in the size of the image when blurred by 1 D. of corneal refractive error is only about 0.2 per cent.

27. Sachs and Meller: Ueber einige eigentümliche Lokalisationsphänomene in einem Falle von hochgradiger Netzhautinkongruenz, Arch. f. Ophth. **57**:1-23, 1904.

been determined independently of the development of the refractive errors. The fact that a partial compensation has occurred does not refute this statement. All or part of the distortions of the dioptric images on the retinas which must take place when the astigmatic errors are corrected by ophthalmic lenses are present and can be measured on the space eikonometer. Thus, the results of this study would be evidence in favor of the Hering theory of the innate and the stable character of corresponding retinal elements.

The results of this study suggest that if patients with astigmatic corrections find difficulty in wearing their corrections, the possibility that aniseikonic errors are present should be investigated.

SUMMARY

The correction of astigmatism at oblique axes introduces a meridional magnification of the dioptric image on the retina at an oblique axis, which, in turn, causes a small rotary deviation of the images of all vertical lines in space. This deviation is designated a declination error, and when it exists between the images in the eyes it can result in an incorrect apparent inclination of objects. Under the test conditions of the space eikonometer this incorrect localization can be measured.

Measurement made on 319 clinical subjects having astigmatism at oblique axes showed that 74 per cent had measurable declination errors in the direction indicated by the axes of the astigmatic corrections. Moreover, there was a good quantitative correlation between the measured declination errors and the declination errors calculated on the basis of the amount and axes of the astigmatism.

This correlation, it is argued, is evidence that the anatomic and physiologic organization of the two retinas in the binocular processes of vision, for the majority of subjects, had become fixed, independent of the development of the ametropic errors. This conclusion presents evidence in favor of the Hering theory of the innate and stable character of corresponding retinal elements.

For the majority of the subjects the measured declination error was less than the error calculated, though for a few subjects it was greater, for some zero and for some in the opposite direction. The difference between the measured and the calculated declination error may be explained by cyclotorsions of the eyes, a basic aniseikonic error, an anomalous organization of the retinas and the existence of a compensatory mechanism.

The evidence suggests that if patients find astigmatic corrections difficult to wear, attention should be given to the possibility that the difficulty may be due to aniseikonic errors resulting from those corrections.

Dartmouth Eye Institute.

CYCLOPIA AND ARHINIA

A NEW CONCEPT

JOSEPH KRAFKA JR., M.D.

AUGUSTA, GA.

In spite of the brilliant researches in experimental embryology, the causal factors concerned with cyclopia in man still remain undetermined. In its most general phases, the problem has been resolved into factors of genesis, organization and mechanics. Nowhere is it clear as to the interrelation of these factors in producing the various degrees of optic and facial defects. Nor has a systematic chronologic investigation been made to determine the sequences necessary to produce the end results.

The department of microscopic anatomy of this university has recently come into the possession of a specimen of cyclopia in a kitten, strikingly different from the 2 specimens of human cyclopia at hand. In the present paper I shall describe the face and the nasal and palatal rudiments as seen in the gross specimen, in roentgenograms and with the clearing method.

Interest in the problem grew as it was realized that the common interpretation of the mechanics of the formation of the philtrum of the upper lip is inconsistent with the existence of the various conditions associated with cyclopia. When the problem is approached from this angle, it is more than a coincidence to find that Mann,[1] in her description of the development of the eye (1928) and in her work on the embryology of anomalies of the eye (1937), came to conclusions which are similar to the theory I have developed here.

One point of difference in our two theories is apparent. Mann maintained that the problem of cyclopia is intimately bound with that of the extension of the visceral mesenchyme of the maxillary processes in reducing the angulation of the two optic primordia. A review of the development of the head shows that this active extension comes at a period much too late to bring about the observed results. There is present, however, a mechanical process at the critical period theoretically capable of producing all the various grades of facial malformation associated with cyclopia.

From the University of Georgia School of Medicine.

1. Mann, I.: (*a*) Development of the Human Eye, London, Cambridge University Press, 1928; (*b*) Developmental Anomalies of the Eye, ibid., 1937.

CYCLOPIA IN A KITTEN

The kitten showing cyclopia was born at full term. The crown-rump measurement was 95 mm. The head measured 25 mm. in the transverse axis and 32 mm. in the longitudinal axis. The eye, occupying the middle of the face, was massive, measuring 10 mm. in height and 11 mm. in width. It was definitely exophthalmic, projecting 6 mm. from the bounding cup. The lens was single, measuring 6 mm. in the vertical axis and 8 mm. in the transverse axis. The pupil was elliptic and sharply angulated at the lateral borders (fig. 1).

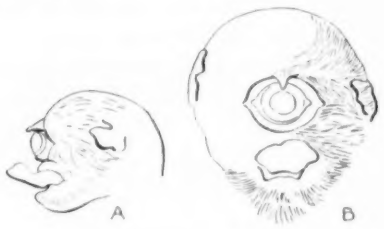

Fig. 1.—Freehand drawing of the head of a cyclopic kitten. *A*, lateral view; *B*, anterior view. Note the snout overhanging the central median eye and the suppression of the upper lip.

A hairy snout, 4 mm. wide and 5 mm. long, was present as a pyramidal projection overlying the upper border of the eye. The lower border of the orbit was formed by a depressed upper jaw. The tongue, apparently normal in size, projected from the oral cavity. The hair lines were normal for the parts involved.

Osteologic Features.—Aberrations in the topographic relations and configurations of the skeletal bones of the face, which are characteristic features of a cyclops (Wright and Wagner [2]), were present in the case of cyclopia in the newborn cat described here. The entire head of this specimen was cleared in potassium hydroxide, and the

2. Wright, S., and Wagner, K.: Types of Subnormal Development of the Head from Inbred Strains of Guinea Pigs and Their Bearing on the Classification of Vertebrate Monsters, Am. J. Anat. **54**:383, 1934.

bones were stained with alizarin red S according to the method of Noback and Noback.[3]

The upper jaw, which normally extends anteriorly to the level of the tip of the mandible, extended in this cyclops to the level between the canine and the first premolar tooth of the lower jaw, or one-fourth the distance from the tip of the normal mandible (fig. 2).

The single median eye and the pyramidal nose above the eye were enclosed by a bony orbit, the upper half of which was bordered by the frontal bones and the lower half by the malar and maxillary bones (fig. 3). The nasal septum, the vomer and the nasal, lacrimal, palatine and ethmoid bones were absent. Except for the frontal bones, all the calvarial bones were apparently normal.

The anteroinferior corners of the paired frontal bones formed a small semicircular recess, in which rested the superior border of the pyramidal nose (fig. 3). The inferior corners of the frontal bones were slightly more inferior than normal, so that the orbital processes formed the entire upper half of the orbit.

The infraorbital process of each malar bone extended medially just short of the midline (fig. 3). The anatomy and articulations of the malar bones, except the articulations with the maxillary bones, appeared normal. Each maxillomalar suture was practically obliterated by the fusion of the two bones (fig. 2). This suture line (figs. 2 and 3), which gives each malar bone normal configuration, was evidenced by an open suture posteriorly, by incomplete fusion endofacially and by a narrow band of intensely red-stained bone along this line ectofacially (alizarin red S has a strong affinity for recently deposited bone [Cameron [4]]). This stained line suggested recent obliteration of the suture.

The remainder of the facial skeleton inferior and medial to the malar bones consisted of (1) two bony plates, one on each side, and (2) a median tubular process (figs. 2 and 3). Each bony plate extended from the maxillomalar line inferiorly to the alveolar border and medially to divide into a superior process, forming the infero-

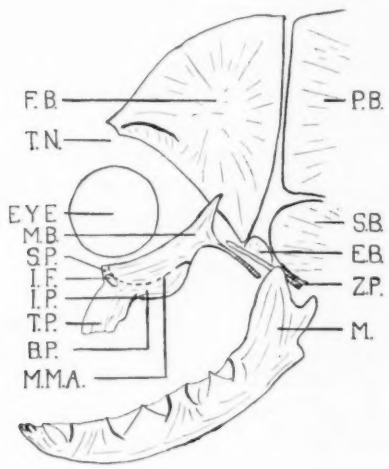

Fig. 2.—Lateral view of the osseous elements in the skull of the cyclopic kitten, as exposed by the clearing method. In this figure, and in figure 3, *B.P.* indicates the bony plate; *E.B.*, ethmoid bone; *F.B.*, frontal bone; *I.F.*, infraorbital foramen; *I.P.*, inferior process of bony plate; *M.*, mandible; *M.B.*, malar bone; *M.M.A.*, maxillomalar articulation (broken line is partially obliterated suture, and solid line is open suture); *P.B.*, parietal bone; *S.B.*, squamosal bone; *S.P.*, superior process of bony plate; *T.N.*, site of pyramidal nose; *T.P.*, tubular process, and *Z.P.*, zygomatic process of the squamosal bone.

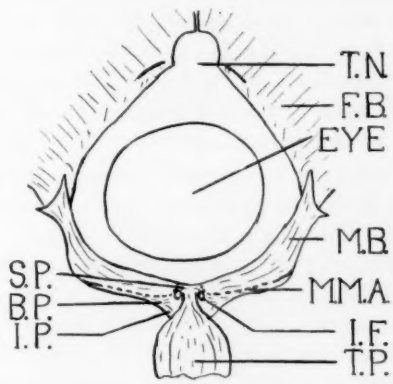

Fig. 3.—Anterior view of the osseous elements in the skull of the cyclopic kitten.

medial border of the orbit, and an inferior process, forming the medioalveolar border. Both processes were fused with their bilateral counterparts at the midline. The alveolar borders had no alveolar processes or teeth. An infraorbital foramen was present. The palatine processes were not developed.

The tubular process extended inferiorly from the circle formed by the bony plate and its processes (figs. 2 and 3). The bony plates and the tubular process were in osseous continuity, with no suture between them. The tubular process enclosed a single median tooth, which had the size and shape of a canine tooth. Structurally the process resembled an alveolar process. Endofacially, a median sliver of bone connected the superior and the inferior process of the bony plate. No intermaxillary suture could be identi-

3. Noback, C., and Noback, E.: Demonstrating the Osseous Skeleton of Human Embryos and Fetuses, Stain Technol. **19**:51, 1944.

4. Cameron, G.: The Staining of Calcium, J. Path. & Bact. **33**:920, 1930.

fied in the midline, either ectofacially or endofacially.

The presence of the infraorbital foramen, the indication of the normal configuration of the lateral margin of the bony plate at the suggested maxillomalar suture line and the lack of any suture lines in the bony plate were strong evidences that each bony plate and its two medial processes were at least part of the malformed maxillary bone. Whether or not the tubular process was derived from the maxillary or from the premaxillary bones is difficult to determine with certainty.

The tubular process may have been of premaxillary derivation. Two reasons may be given in support of this view: 1. The premaxillary bones were normally located in the medial ectofacial aspect of the upper jaw. 2. A suture line may have been obliterated at the junction of the tubular process and the bony plate. Such a line was indirectly indicated by an abrupt change from the thin bone of the tubular process to the thick bone of the bony plate at this junction. If such a suture existed, it could be interpreted as the premaxillary-maxillary suture.

The evidence for the derivation of the tubular process from the maxillary bones is more convincing. Three reasons may be stated: 1. No direct evidence of a suture line existed between the tubular process and the bony plate. In the cat, the premaxillary-maxillary suture persists throughout life. 2. The single median tooth resembled a canine tooth. The canine tooth is normally lodged in the maxillary bone. 3. Presumably, a median nasal process does not contribute to the formation of the upper jaw in a cyclops. As the premaxillary bone develops within the median nasal process, this bone should not appear. Thus the maxillary bone may be interpreted as having developed medially to form the tubular process.

If the tubular process is part of the maxillary bone, as is probable, then the maxillary bone may grow medially to fuse in the midline with its counterpart on the opposite side. However, if the tubular process is derived from the fused premaxillary bones, then these bones may develop without the presence of a median nasal process. In either case the anatomic relation of the tubular process and the bony plates has osteologic significance.

CYCLOPIA AND ARHINIA IN MAN

The first specimen of cyclopia in man is the one purchased for the medical school by Dugas in 1830, and now in the museum of the department of pathology. Its outward features are the same as those of the specimen about to be described, but because of historical value, no attempt was made to study its osteologic features.

The second specimen, that of an infant, born of the fifth pregnancy of a white woman aged 29, was obtained from the University of Georgia School of Medicine Hospital on Nov. 23, 1938. The baby weighed 4 pounds 7 ounces (1.985 Gm.) at birth. It breathed feebly. The heart continued to beat for about one hour.

The brain of this specimen has been fully described by Marburg and Mettler,[5] in 1943. The chief neuropathologic features were reduction in the size of the telencephalon, a cystic diencephalon and agenesis of the corticospinal tracts. A single optic nerve, arising from a median eye, was approximately normal in size.

The head of the cyclops was approximately normal in size and shape. Except for the central eye, three eyelids and the absence of a nose, the facial features were normal. A distinct furrow marked the division between the upper lip and the depression in the nasal area. This furrow extended laterally between the cheeks and the lip. The upper lip showed a typical "cupid's bow," with a tuberculum labii superioris occupying the median segment (fig. 4 *A*). Since this condition indicated the presence of median nasal processes, the question of the presence of a premaxilla arose. After appropriate roentgenograms of the specimen were made, the mouth was opened by lateral cuts and by disarticulation of the lower jaw.

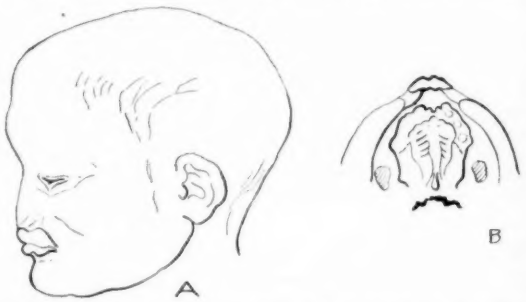

Fig. 4.—Freehand drawing of the head of a human cyclops. *A*, three-quarter view to show the three eyelids, the absence of all nasal rudiments and the well developed philtrum in the upper lip. *B*, inferior view of the palate, showing complete absence of a premaxilla, the normal maxilla and the groove indicating the nasopharynx. The sites of the teeth are indicated by dotted lines; the sectioned mandible, by cross hatching.

The premaxillas were entirely wanting. The maxillary portion of the palate was normal in position and form (fig. 4 *B*). A median raphe

5. Marburg, O., and Mettler, F. A.: The Nuclei of the Cranial Nerves in a Case of Cyclopia and Arhinia, J. Neuropath. & Exper. Neurol. **2**:54, 1943.

terminated in the typical tubercle. Furrows indicated the subdivision of the primary and the secondary palate. The cross striae were prominent. The anterior crescentic border of the alveolar process showed the notch indicative of the incisor foramen. A sharply defined vestibular sulcus set off the arch from the cheeks. A blind nasopharynx was present as an excavation over the posterior border of the hard palate. The soft palate, the uvula and the palatoglossal folds were normal.

To determine the extent of the nasal cavity, one-half the palate was resected, but the cavum extended only as deep as the point beneath the tuberculum. Three well developed teeth, embedded in the alveolar ridges, were exposed; they represented the canine tooth and the first and second deciduous premolars. There was no evidence of the incisors—a fact supported further by the roentgenograms.

Roentgenographic Study of the Human Cyclops.—The following description of the facial skeleton of the infant cyclops in the museum is based on examination of a frontal and a lateral roentgenogram (fig. 5 *A* and *B*). The single median eye was enclosed by a bony orbit, the upper half of which appeared to be bordered by the inferior margins of the calvarial portions of the frontal bones and the lower half by the malar and maxillary bones. Most of the inferior half of the orbit was probably composed of the malar bones, with the maxillary bones forming the portion just lateral to the midline.

Each malar bone had an apparently normal configuration. Each was more medial than normal and thus lay medial to the great wing of the sphenoid bone. As a result, the great wing was excluded from the orbit. The superior border of each malar bone was slightly inferior to the superior border of the great wing of the sphenoid bone.

The frontal process of each maxillary bone was apparently wanting, while the alveolar processes and the anterior nasal spine appeared normal. There was a complement of three teeth on each side.

The vomer, the ethmoid, nasal, lacrimal and palatine bones and the conchae were not visible and were assumed to be absent. Both the osseous and the dental elements of each mandible appeared normal (fig. 5 *A* and *B*).

COMMENT

Embryonic Development of the Normal Face.—The description of the development of the face by His, in 1880, is so simple and convincing that the detail has rarely been called into question. According to this account, the superior medial border of the oral pit is occupied by a frontonasal area; the lateral border, by the area of the first branchial arch, and the inferior border, by the prominence of the developing heart. The lateral margins of the superior border are marked by the prominences produced by the rapidly growing optic cups, which have become stalked at

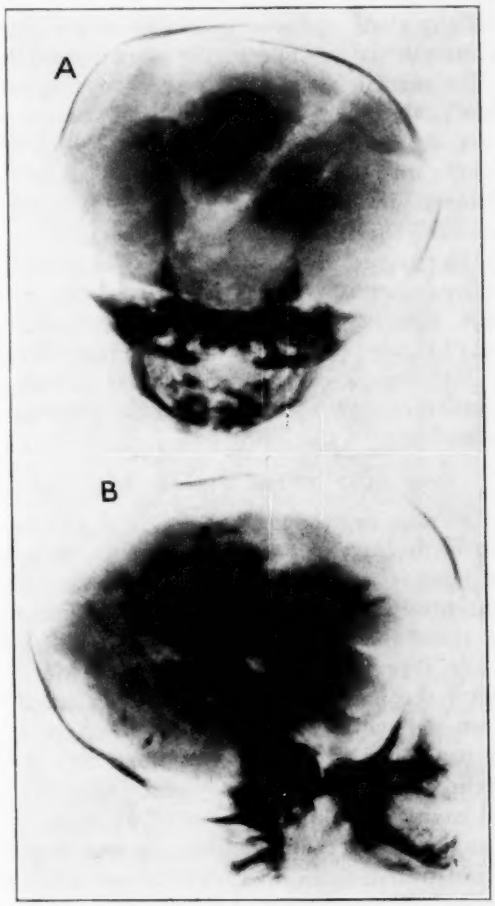

Fig 5.—Roentgenograms of (*A*) the frontal aspect and (*B*) the lateral aspect of the head of the human cyclops.

the 3.6 mm. stage. At the 4 mm. stage a pair of widely separated nasal placodes appear in the ectodermal epithelium slightly medial to and below the optic prominences. At the 6 mm. stage these plates become depressed in the center to form the nasal pits.

The lateral, superior and medial borders of these plates become raised or scrolled, the inferior border persisting as a groove. These primordia have a tendency to move toward the midline. A definite groove sets off the nasal processes from the bulging frontal process above, but not without compression of a median nasal

field between them. In the meantime, the first branchial arch, vertical in position at the 3.6 mm. stage, becomes crescentic, and at the 4 mm. stage it is divided into a dorsal maxillary and a ventral mandibular segment. The superior ends of the maxillary segments grow medially along the border of the oral fossa, coming in contact with the lateral nasal processes, and subsequently with the median nasal processes. The inferior ends of the mandibular processes extend medially along the inferior border of the oral pit to fuse in the midline at the mental symphysis.

The median nasal processes, occupying a median position on the upper border of the oral fossa, develop into the premaxillas, the philtrum and the inferior narial borders. The lateral nasal processes develop into the alae nasi. The median nasal field forms the bridge of the nose.

The fusion of the maxillary processes and the median nasal processes occur at the 8 mm. stage, completing the major steps in the formation of the upper lip and the upper jaw. Lewis,[6] in 1924, reviewed this interpretation of the naso-maxillary angles with regard to the development of the lip.

NOSE AND UPPER LIP IN CYCLOPIA

The nose and the upper lip show a wide variation in the several types of cyclopia. In type 1 the nose is represented by a snout lying above the central median eye. In type 2 a median snout lies above the eye and a harelip is present below it. In type 3 the nose is entirely lacking. In type 4 the nose may be present as a snout between the eye and the upper lip. In type 5 the eye rests on the roof of the mouth, with a typical harelip and a cleft palate present. In type 6 the oral cavity is lacking.

In 5 cases of type 1 the upper lip was described or illustrated as normal (Dutta and De,[7] Der Brucke,[8] Chapman [9] and Mann [1b]). That the snout is a nasal structure has been demonstrated histologically by Dutta and De. In 2 cases of type 2 a harelip existed without any evidence of a premaxilla (Black,[10] Jackson [11]).

Bouman and Schenck,[12] in describing a case of cyclopia of type 3, stated that the "philtrum is lacking." In the 2 specimens of this type in the museum here a well marked philtrum was present, however.

Type 4 is represented in the current literature by a single specimen, that of Mall [13] (no. 559). This is the youngest human cyclops known, being an embryo of 6.5 mm. crown-rump length. It is possible that if development had continued, the snout might have been depressed and produced a cyclops of type 3. Type 5 is represented by Mall's specimen no. 1165. The median eye rests on a cleft lip and palate. Type 6, in which the mouth is entirely closed, is, again, a specimen from the collection of Mall (no. 201). There is a snout between the eye and the brain. Lamb [14] presented a case of cyclopia in a kitten in which both the mouth and the snout were lacking.

There seem to be no special studies on the palate in cases of type 1. Der Brucke [8] stated that in his specimen the nasal bones were lacking, the malar bones were joined in the midline and the palate was fully formed, but he made no statement concerning the premaxillas. Bouman and Schenck's specimen of cyclopia of type 2 corresponded to mine in that the intermaxillary bones and teeth were absent. In the case reported by these authors the philtrum was lacking; in my specimen it was present. There are no data concerning these points in cases of types 3, 4, 5 and 6, but presumably the premaxillas were missing.

THEORIES OF CYCLOPIA

According to the opinion expressed by Wilder [15] (1908), internal or genetic factors are responsible for the development of all grades of teratologic defects. Under his system of Cosmobia, he arranged the various types of ocular and cranial defects into a continuous series of increasing complexity.

The majority of investigators, however, have favored external factors as the effective agents in cyclopia. The philosophic system of St. Hilaire (1832) received support from the experiments of Spemann,[16] in which fusion of the

6. Lewis, F. T.: The Naso-Maxillary Angles—A Disregarded Feature of the Upper Lip, Anat. Rec. (supp.) **27**:209, 1924.

7. Dutta, H. K., and De, N. M.: A Case of Foetus with One Eye, J. Anat. **73**:499, 1939.

8. Der Brucke, M. G.: Cyclopia, Arch. Ophth. **15**: 114 (Jan.) 1936.

9. Chapman, K. H.: Human Cyclopia, Arch. Ophth. **16**:40 (July) 1936.

10. Black, D. D.: The Central Nervous System in a Case of Cyclopia in Homo, J. Comp. Neurol. **23**:193, 1913.

11. Jackson, H.: Cyclopean Monsters: Some General Observations with a Report of a Case, J. A. M. A. **53**:1483 (Oct. 30) 1909.

12. Bouman, K. H., and Schenck, V. W. D.: A Cyclops and a Synotus, J. Anat. **17**:48, 1936.

13. Mall, F. P.: Cyclopia in the Human Embryo, Contrib. Embryol. **6**:5, 1917.

14. Lamb, H. D.: Cyclopia in a Newborn Kitten, Arch. Ophth. **15**:998 (June) 1936.

15. Wilder, H. H.: The Morphology of Cosmobia: Speculations Concerning the Significance of Certain Types of Monsters, Am. J. Anat. **8**:355, 1908.

16. Spemann, H.: Ueber die Entwicklung umgedrehter Hirnteile bei Amphibien Embryonen, Zool. Jahrb. **15**:1, 1912.

two optic primordia was considered to represent the actual mechanism. The investigations of Stockard [17] on the action of magnesium chloride in Fundulus and on resection of the neural plate margin in Amblystoma (1913) indicate that the condition may be best explained on the basis of an agenesis of the median rudiment of the neural plate, which prevents the lateral migration of the optic anlage.

Postulates of historical interest held responsible for cyclopia in man are the premature closure of the neuropore (Dareste), intercranial pressure (Ahlfeld) and early arrest in a phylogenetic stage (Naegeli). Winchler expressed favor toward the view of hypdrops of the third ventricle.

The theory of maternal endocrine disturbance, while not clearly expressed, has been intimated by several investigators who observed a variability of anomalies in successive pregnancies. Van Duyse's case (cited by Mall) is of interest. The first child born to a woman who had had four abortions showed a harelip; the second, a cleft palate; the third was normal, and the fourth, twin to a normal baby, was a cyclops. In Jackson's [11] case a cyclops was born twin to a normal child. The other children of this mother were normal. Whether or not the twins were monozygotic is not stated. At any rate, these cases seem to rule out the effect of endocrine influences from the mother.

The theory of the amnionic band, premised to explain many types of anomalies, is not applicable to cyclopia, since its effect would be to separate the optic rudiments, rather than to bring them together.

Mann's [1b] theory of cyclopia is unique in that she premised a specific mechanical factor responsible for this condition. She stated:

> . . . The fusion of the eyes can morphologically be looked upon as an excessive amount of normal gradual reduction of the angle between the two optic stocks, the mechanism of which is bound up with the growth of the maxillary processes.

Her statement in 1928,[1a] however, introduced ambiguity into the problem.

> . . . This reduction in angle is normally arrested by the midline structures, but since in cyclops these are never fully developed, the optic areas are from the beginning nearer together, even before the extension of the maxillary processes.

In her work on the normal development of the eye,[1a] she discussed at length the factors responsible for the reduction of the optic angle, which at the 9 mm. stage is 160 degrees; at the 16 mm. stage, 120 degrees, and at the 40 mm. stage, 72 degrees. I shall revert to this concept in a subsequent discussion.

Adelmann,[18] using the technic of the experimental embryologist, expressed himself in favor of the view that the factor responsible for cyclopia is not so much a defect in the optic anlage of the neural plate as one in the underlying substrate of prochordal mesenchyme. If this concept were correct, it would be difficult to see how a normal oral region could occur in the presence of cyclopia. Further, it would preclude the occurrence of an anterior lobe of the hypophysis, which is occasionally observed.

CHRONOLOGIC DEVELOPMENT OF STRUCTURES INVOLVED IN CYCLOPIA AND ARHINIA

Optic Sulci.—The earliest stage at which the optic rudiments may be definitely recognized is the 8 somite (2.3 mm.) stage (Bartelmez [19]) in which they occur as thickenings of the margin of the neural plate marked by grooves. Corner [20] gave a good description of them at a 10 somite stage (2.6 mm.) and identified a torus opticus between them. The optic rudiments have become slightly raised by evagination along these grooves at the 16 somite stage and have become definitely stalked at the 20 somite stage (Wen [21]). They are bulbar at the 24 somite, or 3.6 mm., stage (Johnson [22]). The choroid fissure, appearing at the 4 mm. stage, is invaded by the hyaloid artery at the 6 mm. stage.

Lens.—The lens appears as a thickening in the surface epithelium in the proximity of the optic cup at the 4 mm. stage. At the 7 mm. stage it has invaginated and become a free vesicle. The proliferation of the posterior epithelium to become the lens fibers is in progress at the 12 mm. stage, and the vesicle becomes solid at the 14 mm. stage. The lens becomes surrounded by the lips of the optic cup at the 14 mm. stage, as the choroid fissure is obliterated.

Accessory Optic Structures.—The muscle mass for the extraocular muscles is present at the 8 mm. stage and begins to differentiate into specific muscles at the 10 mm. stage. The ciliary

17. Stockard, C. R.: An Experimental Study of the Position of the Optic Anlage in Amblystoma Punctatum, with a Discussion of Certain Eye Defects, Am. J. Anat. **15**:253, 1913.

18. Adelmann, H. B.: The Problem of Cyclopia, Quart. Rev. Biol. **11**:161, 1936.

19. Bartelmez, G. W.: The Origin of the Otic and Optic Primordia in Man, J. Comp. Neurol. **62**:81, 1922.

20. Corner, G. W.: A Well Preserved Human Embryo of Ten Somites, Contrib. Embryol. **20**:81, 1929.

21. Wen, I. C.: The Anatomy of Human Embryos with 17 to 23 Pairs of Somites, J. Comp. Neurol. **45**: 301, 1928.

22. Johnson, F. P.: A Human Embryo of Twenty-Four Pairs of Somites, Contrib. Embryol. **6**:127. 1917.

ganglion is present at the 14 mm. stage. The cornea and the anterior portion of the sclera are specific at the 12 mm. stage, but the posterior half of the sclerotic vesicle is not differentiated until the 20 mm. stage. These points are of interest with respect to the variability in fusion of the two potential eyes within a single sclerotic coat. Chapman [9] reported fusion of the posterior halves of the eyes in 12 out of 16 cases.

Optic Nerve.—The presence of a single optic nerve, with or without an attempt at production of a chiasm, depends on the degree of fusion of the optic cups and on the status of the torus opticus. The fibers in the optic nerve are commonly described as passing from the retina to the brain and as reaching the optic chiasm at the 20 mm. stage. Hence the condition of the optic nerve follows a primary cyclopia.

Nasal Placodes.—The nasal placodes, like the lens, are fairly late in development. They first appear at the 4 mm. stage as thickenings in the surface ectoderm at the lateral borders of the stomodeal wall. They seem to be entirely autonomous in origin, although it has been observed that four placodes may be formed in experimental cyclopia, owing to underlying structural defects.

At the 6 mm. stage the placodes invaginate and the nasal pits are formed, a process producing simultaneously the median and the lateral nasal processes. At the 8 mm. stage the maxillary processes have extended along the upper border of the stomodeum and have fused with the median nasal processes. This establishes the premaxillas internally.

The bucconasal membrane becomes perforate at the 18 mm. stage. The median nasal septum is free from the maxillary palatal processes at all points except around the primitive incisor foramens. The lateral walls of the nasal cavity begin to show turbinate formation at this period.

Olfactory Nerve and Olfactory Lobe.—A description of the olfactory nerve and the olfactory lobe is wanting in cases of cyclopia. Presumably they are absent. The probable reason is that of late development, the abnormal ocular condition interfering with their correlated differentiation. The olfactory nerve is formed by axonic ingrowths from the nasal placodes (Pearson,[23] Humphrey [24]), and the growth of the olfactory lobe is due to this stimulus. The lobes are first recognizable at the 9 mm. stage (Papez [25]).

Brain and Ventricular System.—In the 10 somite specimens of Corner closure of the neural groove has just begun at the hindbrain. The neural tube is complete in the brain region at the 17 somite stage at all points except the anterior neuropore (Atwell [25a]). The fourth ventricle has assumed the typical thin-walled roof. The neuropore is open in Bremer's [26] 4 mm. specimen but is closed in Wen's. The cerebral vesicles begin to assume a bulge at the 8 mm. stage. The ridges representing the primordia of the corpora striata underlie the interventricular foramens, but the area in the lamina terminalis remains undifferentiated. The pontile flexure does not occur until the 12 mm. stage.

It is evident from this review that the closure of the anterior neuropore comes too late to produce an internal hydrocephalus or hydrops of the third ventricle capable of bringing about cyclopia.

NEW CONCEPT OF THE MECHANISM OF CYCLOPIA

Intrigued by the theory of maxillary extension which I developed before I was aware of this concept of Mann, I checked on the conditions of the first branchial arch during the formative period in which cyclopia arises. That this period is early, i. e., before the 24 somite stage, is to be deduced from the status of the lens and the olfactory plaques in this condition. There is also factual evidence that cyclopia arises early, since the specimen of Mall is but 6.9 mm. in length.

In the Payne [26a] embryo, of 7 somites and 2.17 mm. in length, the first branchial arch is clearly indicated. In the Corner specimen,[20] of 10 somites, it is wide and oblique. In the Atwell specimen [25a] it has become constricted and is assuming a vertical angle. At the 3.6 mm., or 24 somite, stage the Johnson specimen [22] shows the beginning of the division of the first arch into a maxillary and a mandibular segment. At the 4 mm. stage the mandibular segment has proliferated to the extent of forming the mental symphysis.

23. Pearson, A. A.: The Development of the Nervus Terminalis in Man, J. Comp. Neurol. **75**:39, 1941.

24. Humphrey, T.: Development of the Olfactory and Accessory Olfactory Formation in the Human Embryo and Fetuses, J. Comp. Neurol. **73**:431, 1940.

25. Papez, J. W.: Embryologic Development of Hypothalamic Area in Mammals, A. Research Nerv. & Ment. Dis., Proc. (1939) **20**:31, 1940.

25a. Atwell, J. M.: A Human Embryo with Seventeen Pairs of Somites, Contrib. Embryol. **21**:1, 1930.

26. Bremer, J. L.: Description of a 4 mm. Human Embryo, Am. J. Anat. **5**:459, 1906.

26a. Payne, F.: General Description of a 7 Somite Human Embryo, Contrib. Embryol. **16**:115, 1925.

Branchial groove I and arch II are indicated in the Corner embryo; groove II and arch III, in the Atwell specimen, and groove III and arch IV, in the Johnson form. This differentiation indicates great activity in the region, but some other factor that is effective at or before the optic grooves differentiate must be sought, i. e., some agent near the anterior end of the embryonic shield at the time of formation of the first somites.

Examination of the Ingalls [27] embryo (1920), length 1.38 mm., in which the first somites are seen, shows that the first branchial arch is invaded by the first aortic arch, lying in contiguity with the anterior end of the head fold and the neural plate.

In the Payne specimen (7 somites) the aortic arch plexus is extremely dilated and massive. It is somewhat reduced in the Corner embryo. In the Atwell specimen the second arch has appeared, but it does not attain any great size. In the Johnson specimen aortic arches I and III are present as vascular channels of equal size. In the Bremer [26] embryo arches I and II have begun to atrophy (Congdon [28]).

While a cardinal venous plexus has begun in the Payne embryo, it is still detached in the Corner embryo. This plexus establishes continuity in the Atwell specimen, draining into the sinus venosus. This drainage may be responsible for the reduction in size of aortic arch I, since it would relieve vascular tension in this vessel.

It is evident that angiogenesis in this area is very active at the time of the premised period during which the optic rudiments are forming. Normally, the two plexuses representing the first aortic arches remain separate in the head region. However, should they fuse across the midline of the body, they could produce a traction factor against which the optic rudiments, in their movement from the midline, would have to act. This, a simple mechanical factor, could produce the necessary conditions capable of bringing about all grades of cyclopia. Vascular variability, a common occurrence in production of defects in other regions of the body, must occasionally occur here. This concept provides the mechanics of the substrate defect premised by Adelmann, without the objections previously raised.

With the primary factor of cyclopia once established, it is apparent that a single median eye may be directed toward the head ectoderm at three levels: (1) below the site of formation of the nasal placodes, (2) at the level of the site and (3) above this level. In the first instance, a nasal snout may develop above the eye and a harelip may be an accompanying feature. In the second instance the snout may lie above the eye and a typical premaxilla and a tuberculum be present. In the third instance the snout may lie below the eye or be completely suppressed, with or without a tuberculum.

The interpretation of the origin of the philtrum becomes an important feature in analysis of the aforementioned conditions. If the tuberculum is derived from the frontonasal processes, it is difficult to conceive of a factor which would retain the lip and suppress the premaxillas, since the labiogingival groove subdividing this area at the 6 mm. stage appears at a time when the primary factors of cyclopia have passed. It is of course possible to interpret the tuberculum and philtrum as the result of the development of the invading maxillary mesenchyme (Frazer [29]). But since this invasion, as described by Frazer, does not occur until the 13.5 mm. stage, it would seem that all cyclops should have normal lips. Since Frazer's account is not widely known, I quote from his work as follows:

> . . . The thick mass [maxillary mesoderm] which thus comes to be placed in front of the original frontonasal process provides the mesodermal bed in which, in its deeper portions, the bony alveolus of the premaxillary region is laid down; in its superficial part it makes the lip. . . . The philtrum appears to be formed by the meeting of the masses of mesodermal invasion in the lip region [page 295]. . . . The extension of maxillary mesoderm—between the narial apertures and the mouth . . . forms the upper lip and the alveolus . . . covering the facial aspect of the fronto-nasal processes and hiding it completely so that it is not concerned in the formation of the facial surface [page 288].

Johnson,[30] Derry [31] and Jones [32] lent supportive evidence to the theory of maxillary extension and claimed that the processes encroach on the nasal rudiments and form the floors of the narial borders. They further maintained that the maxillas form the anterior aspects of the incisor alveoli, reducing the premaxillas to the posterior walls of the sockets.

27. Ingalls, N. W.: A Human Embryo at the Beginning of Segmentation with Special Reference to the Vascular System, Contrib. Embryol. **11**:61, 1920.

28. Congdon, E. D.: Transformation of the Aortic Arch System During the Development of the Human Embryo, Contrib. Embryol. **14**:47, 1922.

29. Frazer, J. E.: A Manual of Embryology, Baltimore, Williams & Wilkins Company, 1941.

30. Johnson, E. H.: The Narial Margin in Man, J. Anat. **71**:356, 1937.

31. Derry, D. E.: Two Skulls with Absence of Premaxillae, J. Anat. **72**:295, 1938.

32. Jones, F. W.: The Fate of the Human Premaxilla, J. Anat. **72**:462, 1938.

All these extensions, however, come too late to explain the supraocular, subocular and suppressed nasal rudiments seen in cases of cyclopia.

As previously stated, Mann based her view of the cause of cyclopia on the reduction of the optic angle. To check this point further in an attempt to establish the effect of maxillary ingrowth, I made measurements of the internarial angle during this period on models of embryos in the collection at this university.

Stage	Internarial Angle, Degrees
At 7.5 mm.	140
At 18 mm.	18
Adult	10

The shift of the olfactory placodes is thus seen to be entirely independent of the factor which produces the reduction in the interocular angle. Frazer postulated that such a rotation of nasal rudiments is due to the pressure of growth of the cerebral hemispheres, but the condition of the brain between the 7.5 and the 18 mm. stage hardly justifies such a conclusion. Certainly, the supraocular position of the nasal snout in cases of cyclopia presents an unsurmountable difficulty in any such interpretation. That the internarial tissue acts as a tension factor keeping the nasal rudiments near the midline is evident, but the initial actual and relative reduction of the internarial space remain unexplained.

CONCLUSIONS

In 2 cases of cyclopia, 1 of a human infant and 1 of a kitten, the osseous elements were studied roentgenographically and by the clearing method to determine the role of the premaxillas in lip formation.

Current theories on the mechanics of cyclopia fail to discover the factors responsible for the development of various grades of cyclopia and associated oral and nasal defects.

The Frazer-Mann maxillary extension theory is reviewed specifically and is shown to be inadequate as an explanation of cyclopia.

A vascular tension theory involving the fusion of the first aortic arches in the midline is premised as fulfilling the conditions required for the development of all grades of cyclopia and arhinia.

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OCULAR DEFECTS IN SIXTY THOUSAND SELECTEES

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The physical examination of selectees to determine acceptability for induction into the armed forces affords a unique opportunity for estimating the incidence of various ophthalmic conditions in a comparatively large and statistically significant group of men. This study consists of an analysis of the results of my examination of 60,000 men, a consecutive series, at an armed forces induction station.

MATERIAL AND METHOD

These men represented an age group of from 18 to 38 years, together with a few enlistees aged 17 and selectees between 38 and 45 years of age. Thus, ophthalmic conditions peculiar to childhood, puberty and senescence were not encountered. In addition, preliminary "screening" examinations, performed by physicians at the various local selective service boards, eliminated from the group some who were obviously visually unfit. It is readily apparent, therefore, that the incidence of the various conditions recorded here can be applied only to a comparable group, and not to the population at large.

Of the 60,000 men in this series, 5,712 (9.5 per cent) were found to have ophthalmic defects. Data were accumulated in the course of the complete physical examination for induction, and not from a mere analysis of records. This was accomplished by entering each defect as encountered in the appropriate column of a large chart easily accessible to the examining ophthalmologist. From these data the accompanying tables were derived. In the tables is given the ratio of relative incidence for each condition, this ratio representing the frequency with which each abnormality was noted. Thus, the ratio for all ophthalmic defects is 1 : 10.5; in this series, 1 of each 10 or 11 men examined was found to have some ocular defect.

Percentages, whenever used, are based on the total number of selectees examined, namely, 60,000, except when otherwise noted. The words "above" and "below" when used with reference to visual acuity are equivalent to "better than" and "poorer than" respectively, according to common ophthalmologic usage. The term "amblyopia" refers to central visual acuity below 20/40 with the best possible correcting lenses, as determined by methods of refraction, in the absence of organic disease.

Many rare ocular abnormalities were encountered in this large series of subjects. These unusual conditions have been listed separately in the tables, in order to render available figures for the incidences of some of the rarer abnormalities.

The ophthalmologic examination of each man was made methodically and according to a definite plan. The visual acuity of each eye was tested separately, with and without glasses. Poor uncorrected central visual acuity indicated use of the methods of refraction or of the stenopaic opening to improve, if possible, the acuity to an acceptable level. Tests for the detection of malingerers were used in suspected cases. Experience gives the examining ophthalmologist the ability to detect something indefinably characteristic in the bearing and manner of the visual malingerer. The tests employed involved the use of vertical or horizontal prisms, various trial lenses in the trial frame and variations in the test charts or in the distance at which they were read. The status of each suspected malingerer was carefully evaluated by the neuropsychiatric section before the final decision was made.

The ocular adnexa and anterior segments were examined for the presence of anomalies, injury and disease. The extraocular movements were tested, and strabismus was noted if present; routine examination of the ocular muscle balance, with the cover test or the Maddox rod, was not done except when indicated. The reaction of the pupils to light and in accommodation was tested. The ophthalmoscope was employed for the remainder of the examination. A convex lens with a strength of 10 to 20 D. was used to examine the cornea and iris, and both fundi were inspected, with particular attention to the optic papilla, the blood vessels and the retina. Dilation of the pupil with homatropine was necessary at times for careful examination of the central region of the fundus oculi, as well as in some cases of lenticular opacity and retinal detachment. Other procedures were only occasionally necessary. The peripheral and central visual fields were determined when indicated; tension was taken by tactile means when the presence of glaucoma or hypotony was suspected, and transillumination of the globe was carried out in most cases of detached retina. Diplopia fields were investigated by means of a red glass in cases of paralysis of extraocular muscles.

Whenever any selectee required more time for ophthalmologic investigation than could be taken at the original examination, he was detained until an adequate study of the ocular abnormality could be made. The entire examination of each man was performed personally by me except for the preliminary testing of the visual acuity, which was done by an assistant under direct supervision. The examination was solely diagnostic, to determine the acceptability of the selectee for military service under the current mobilization regulations.

RESULTS OF ANALYSIS

Refractive Errors.—Selectees with uncorrected visual acuity below 20/200 due to refrac-

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tive errors totaled 2,032, or 3.4 per cent of the entire series (table 1). Myopia, with and without associated astigmatism, was the cause in 93 per cent of cases of defective vision due to refrac-

TABLE 1.—*Incidence of Refractive Errors in a Series of 60,000 Selectees*

	Total No.	Ratio
Myopia, below 20/200 to 20/400	1,525	1:40
Myopia, below 20/400	362	1:166
Myopia, high, unilateral	48	1:1,250
Hypermetropia, below 20/200 to 20/400	71	1:845
Hypermetropia, below 20/400	26	1:2,305
	2,032	1:30

tive errors. The low figures for hypermetropic errors are probably due to the relatively high accommodative power present in persons of this age group.

Forty-eight cases of high unilateral myopia were encountered. This comparatively infrequent condition is not strictly refractive but is included in this category. In all 48 cases one eye was essentially normal whereas the fellow eye was highly myopic, to the extent of 10 D. or more, and usually gave the appearance of unilateral exophthalmos.

Strabismus.—Of the total number of men examined, 1,245, or 2 per cent, had manifest strabismus (table 2). The number of cases of convergent types was 855, and the number of cases of divergent types was 389. Amblyopia ex anopsia was an associated condition in 1,066 of the 1,245 cases of manifest strabismus. Further, amblyopia ex anopsia was encountered much more frequently in conjunction with convergent strabismus than with divergent strabismus; it was an associated condition in 90 per cent of the cases of esotropia, whereas it was present in only 60 per cent of the cases of exotropia.

TABLE 2.—*Number of Selectees with Strabismus in Series of 60,000*

	Total No.	Ratio
Esotropia, with amblyopia	770	1:78
Esotropia, without amblyopia	85	1:706
Exotropia, with amblyopia	296	1:202
Exotropia, without amblyopia	93	1:646
Right hypertropia	1	
	1,245	1:48

In this series, two factors bear on the incidence of strabismus. First, only cases of manifest strabismus are included. Thus, cases of strabismus in which treatment had been effective either by prescription of glasses or by operative intervention and cases in which the deviation had disappeared spontaneously as the patient reached adulthood are not classified here as instances of strabismus. Second, as previously stated, complete examination to determine the exact degree of ocular muscle balance was not done routinely, and thus it is possible that a small number of cases of the alternating type of strabismus with normal central visual acuity in each eye, and with deviation of low degree, were overlooked. However, the presence of poor visual acuity with appropriate correcting lenses (amblyopia) not accounted for by the presence of organic disease always required further investigation, including examination of the muscle balance, and thus associated strabismus of low degree would then be noted when otherwise it might not have been observed. In table 6 are listed 855 cases of amblyopia with which strabismus was not associated. In many of these cases, although not listed separately, there was a history of strabismus in childhood. Manifest strabismus was never present, however, and for this reason all the cases have been excluded here.

Right hypertropia of unusual severity (30 degrees) was noted in a selectee aged 24. Neither amblyopia ex anopsia nor diplopia was associated, and the condition had been present since birth.

Paralysis of Extraocular Muscles.—Paresis or paralysis of the extraocular muscles was an infrequent finding; 24 cases were noted, a ratio of incidence of 1:2,500. Unilateral paralysis of the sixth nerve was the most frequent, occurring in 17 cases; bilateral congenital paralysis of this nerve was noted only once. Paralysis of the superior oblique muscle accounted for 3 cases; paralysis of the third nerve, for 1 case, and isolated paralysis of the right superior rectus muscle, for 1 case. A selectee aged 32 had complete, bilateral internal and external ophthalmoplegia, which had followed a basal fracture of the skull six years before.

Optic Nystagmus.—There were 80 cases of idiopathic optic nystagmus in this series, a ratio of incidence of 1:750. In all these cases the nystagmus was of the pendular type with the subject in the "eyes front" position. Vestibular types of nystagmus, nystagmoid movements and nystagmus associated with neurologic conditions were encountered, but cases of these forms have not been included in this series. Bilateral amblyopia (defined here as corrected vision below 20/40) was associated with the nystagmus in 44 of the 80 cases.

Two interesting cases of monocular nystagmus were encountered. In both cases one eye was normal in all respects. The affected eye in each case showed spontaneous pendular nystagmus.

In 1 case it was associated with unilateral myopia of high degree, and the nystagmus was horizontal. In the other instance the nystagmus was observed in a previously injured eye in which post-traumatic aphakia was present; the monocular nystagmus was peculiar in that it was both vertical and rotatory.

Congenital Anomalies.—The many and varied types of anomalies encountered are listed in the tables, together with the other defects of the structures of the eye concerned.

External Ocular Abnormalities.—Disorders of the adnexa and the external parts of the eye were seen in 294 cases, a ratio of incidence of 1:203 (table 3). Active trachoma was rare,

TABLE 3.—*Number of Selectees with External Ocular Abnormalities in a Series of 60,000*

	Total No.	Ratio
Corneal scars, acuity below 20/40	93	1:645
Blepharoptosis	46	1:1,300
Active trachoma	25	1:2,400
Pterygium	23	1:2,610
Interstitial keratitis	14	1:4,280
Microphthalmos, unilateral	12	1:5,000
Dermoid	10	1:6,000
Keratitis, miscellaneous types	10	1:6,000
Albinism	8	1:7,500
Conjunctivitis, chronic, severe	8	1:7,500
Blepharitis marginalis	7	1:8,570
Keratoconus	5	1:12,000
Dacrocystitis, chronic	4	1:15,000
Epicanthus, marked	3	1:20,000
Exophthalmos, thyrotoxic	3	1:20,000
Conjunctivitis, acute, severe	3	1:20,000
Lacrimal fistula	2	1:30,000
Loss of one eye, ophthalmia neonatorum	2	1:30,000
Tarsectomy, post-trachoma	2	1:30,000
Microphthalmos, bilateral	2	1:30,000
Other conditions *	13	
	295	1:203

* One case each of conjunctival hemangioma, blepharochalasis, congenital corneal opacity with embryotoxon, vernal conjunctivitis, senile ectropion, episcleritis, juvenile glaucoma, hypertelorism, lye burns of the orbit, benign melanoma of the caruncle, ocular pemphigus, blepharoptosis with hemangioma and severe post-traumatic orbital scarring with exotropia.

despite the comparatively large number of American Indians examined. In many instances the lids showed old conjunctival scarring, and in 2 cases corrective tarsectomy had been done, but only 25 cases of active trachoma were encountered. In 14 cases corneal nebulas due to healed interstitial keratitis were noted. In 6 cases visual acuity was 20/40 or better in each eye. In the entire series, there were encountered only 8 cases of severe chronic conjunctivitis, 3 cases of severe acute conjunctivitis and 1 case of palpebral vernal conjunctivitis. Keratoconus was noted in 5 cases; in 2 of these cases the condition was in an early stage, and visual acuity with correcting lenses was 20/40 or better in each eye. Congenital anomalies involving the eye as a whole are noted here for convenience. These include unilateral microphthalmos, in 12 cases; bilateral microphthalmos in 2 cases, and albinism, in 8 cases. One case of juvenile glaucoma is also included. One eye had previously been removed, and there was notable constriction of the visual field with corrected central visual acuity of only 20/70 in the remaining eye.

Iris.—In 41 cases, a ratio of 1:1,460, lesions of the iris occurred as the ocular defect of primary importance. The lesions of the iris usually present in eyes undergoing involuntary changes due to destructive injury or disease are not included here.

An interesting case encountered was that of a cystic malignant melanoma of the root of the iris in a selectee aged 20. The left eye was profoundly amblyopic and could perceive only light and motion. In the right eye a round, yellow, cystic mass, 6 mm. in diameter, arose from the medial root of the iris and encroached on the pupil; on initial examination this was thought to be an inclusion cyst, as a history of previous trauma was elicited. The selectee was advised to see a surgeon, and later the entire cyst, including the root of the iris, was successfully removed. Examination of a microscopic section of the tumor showed clusters and masses of comparatively large, pale and maculated cells, which were in part spindle shaped. Mitotic figures were not seen in any part. There was, however, a large amount of dark pigment. A pathologic diagnosis of malignant melanoma of the iris was made. This selectee was alive and well, with vision of 20/20 in this eye, one year after the operation.

In another case the presence of sympathetic ophthalmia was suspected. The man, aged 30, had sustained a penetrating injury of one eye fourteen months previously. Severe plastic uveitis was present in each eye, with pronounced visual impairment.

The remaining lesions of the iris encountered in this series consisted of iridodialysis, 7 cases; anterior synechia, 6 cases, and iridocyclitis, 5 cases, with aniridia, post-traumatic aniridia, bilateral essential atrophy of the iris, post-traumatic coloboma of the iris, iris bombé, iridocyclitis with secondary glaucoma, benign melanoma of the iris and post-traumatic coloboma of the lens and iris, in 1 case each. In 13 cases congenital coloboma of the iris was also encountered. In 7 of these cases the condition occurred in conjunction with coloboma of the choroid; in 4 cases, independently of other ocular defect, and in 2 cases, in association with coloboma of the lens.

Lens.—Abnormalities of the crystalline lens of the eye were encountered in 257 cases

(table 4). Cases of traumatic and secondary cataract, such as is usually found in eyes subject to involuntary changes following extensive injury or disease, were not included in this total.

TABLE 4.—*Incidence of Abnormalities of Lens in a Series of 60,000 Selectees*

	Total No.	Ratio
Cataract, traumatic	107	1:560
Cataract, congenital	45	1:1,330
Cataract, secondary	18	1:3,330
Aphakia, operative, monocular	35	1:1,700
Aphakia, post-traumatic	14	1:4,280
Aphakia, operative, bilateral	9	1:6,660
Traumatic dislocation of lens	12	1:5,000
Ectopia lentis	9	1:6,660
Coloboma of lens and iris	2	1:30,000
Other conditions *	6	
	257	1:233

* One case each of cataract due to lightning, sunflower cataract in a case of chalcosis, partial cataract with post-traumatic coloboma of the lens and iris, operative aphakia with myopic chorioretinitis, traumatic central chorioretinitis and bilateral microphthalmos.

Of the 257 instances of lenticular lesions, 173 were of cataract, whereas a relatively high number, 61, were of aphakia, either operative or post-traumatic. In 14 cases of post-traumatic aphakia there was no history of operative intervention. Apparently, the original injury had ruptured or perforated the lenticular capsule, so that complete dissolution of the lenticular substance resulted.

A selectee aged 28 had had bilateral discission for high myopia. The pupillary apertures were clear, and the residual myopic error was approximately 5 D. However, the corrected visual acuity was only 20/200, owing to severe myopic chorioretinitis. In another case a man aged 30, 1 of the 2 selectees with severe bilateral microphthalmos in this series, had a history of bilateral discission for congenital cataracts at the age of 4 years. Useful vision of 20/200 was obtained in each eye with convex lenses of 16 D., and the man was successful as a farmer in spite of what is usually an ocular defect causing total visual incapacitation. Another unusual case was that of a man aged 21 who had suffered a laceration of the right eye at the age of 1 month. Examination showed a horizontal linear scar at the junction of the middle and the upper third of the cornea. The entire upper third of the lens and iris of this eye was absent. Below the aphakic region thus formed the lens was opaque for a distance of about 1 mm., and visual acuity through the comparatively clear lower half of the lens was 20/40. Two other unusual cataracts were seen, 1 a sunflower cataract associated with chalcosis and the other a monocular cataract which had developed within a few months after the man, at the age of 23, had been struck by lightning.

Vitreous.—Abnormal conditions of the vitreous body were noted in 17 cases, a ratio of 1 : 3,550. In 10 of these cases there was synchysis with hematogenous pigmentation following old injuries. Four cases of recent traumatic hemorrhage into the vitreous body were seen. In 1 otherwise normal eye a persistent blood-carrying hyaloid vessel arose from the disk, came forward to the posterior surface of the lens and disappeared downward toward the ciliary body. In 1 case there was a history of repeated hemorrhages into the vitreous body of one eye, verified by a letter from the man's own physician. No abnormality of the retinal vessels could be seen, but there was a diffuse haze in the vitreous. In another case a large, flat, pigmented, spider-shaped floater, approximately twice the size of the optic disk, was present in the vitreous body of an otherwise normal eye, about 5 D. anterior and nasal to the optic disk, moving slightly on movements of the eye.

Optic Nerve.—The optic nerve showed abnormalities in 53 cases, ratio of 1 : 1,132. In 45 of these cases there was optic nerve atrophy of some form. In 25 cases a definite history of blindness in one eye following trauma, usually basal fracture of the skull, was obtained, and for this reason the blindness in these cases is called post-traumatic; in 15 cases no definite etiologic factor could be determined. Three cases of hereditary optic atrophy were encountered; in each case a history of familial incidence was elicited. In 1 case of proved multiple sclerosis partial atrophy of both optic nerves was present, and in 1 case of atypical optic nerve atrophy healed central chorioretinitis was encountered.

Papilledema was seen in 2 cases, in both of which the presence of cerebral tumor was suspected. Optic neuritis was observed in a solitary case, in one eye of a man who had also bilateral, moderately advanced retinitis pigmentosa. Three cases of severe pseudoneuritis were noted, all associated with hypermetropia. A case of coloboma of the optic nerve and another of coloboma of the optic disk were seen.

Retina and Choroid.—Abnormalities of the retina and choroid formed a large and varied series, difficult to classify satisfactorily. The 374 cases have been grouped into five categories: anomalies, 160 cases; generalized diseases of the retina and choroid, 60 cases; abnormalities of the central region, 97 cases; retinal detachment and closely allied conditions, 38 cases, and typical myopic chorioretinitis, 19 cases (table 5).

In the first group, that of congenital anomalies, the diagnosis of tuberous sclerosis (Bourne-

ville's disease) was made in 2 cases on the basis of the presence of the typical retinal tumor. In both cases, neurologic signs were present, and adenoma sebaceum of the face was associated.

TABLE 5.—*Incidence of Abnormalities of the Retina and Choroid in a Series of 60,000 Selectees*

	Total No.	Ratio
Anomalies		
Medullated nerve fibers	140	1:428
Coloboma of choroid	12	1:5,000
Colloid bodies	2	1:30,000
Melanoma of fundus, benign	2	1:30,000
Tuberous sclerosis	2	1:30,000
Other conditions *	2	
	160	1:375
Generalized disease		
Choroiditis, cause undetermined	20	1:3,000
Retinitis pigmentosa	14	1:4,280
Chorioretinitis disseminata	7	1:8,570
Choroidal sclerosis	4	1:15,000
Healed choroidal rupture	4	1:15,000
Post-traumatic retinopathy	4	1:15,000
Coats's disease	2	1:30,000
Other conditions †	5	
	60	1:10,000
Central		
Central chorioretinitis, post-traumatic, healed	50	1:1,200
Central chorioretinitis, healed	24	1:2,500
Batten-Mayou disease	11	1:5,460
Solar retinopathy	11	1:5,460
Other conditions ‡	1	
	97	1:620
Retinal detachment		
Post-traumatic	18	1:3,330
Complicated	7	1:8,580
Successful operative repair	6	1:10,000
"Idiopathic"	5	1:12,000
Other types §	2	
	38	1:1,580
Myopia		
Unilateral with myopic chorioretinitis	9	1:6,660
Chorioretinitis, with high myopia	8	1:7,500
Other types ‖	2	
	19	1:3,150
	374	1:160

* One case each of choroideremia and von Hippel-Lindau disease.

† One case each of chorioretinal atrophy with glaucoma, circinate retinopathy, Eales's disease, chorioretinitis due to metallic copper, and "salt and pepper" fundus.

‡ One case of presenile bilateral macular degeneration.

§ One case each of congenital nonattachment of the retina with microphthalmos and unsuccessful operative repair of retinal detachment.

‖ One case each of bilateral myopic chorioretinitis and aphakia and unilateral myopic chorioretinitis with unilateral myopia of only 3 D.

An interesting case of von Hippel–Lindau disease (combined hemangioma of the cerebellum and retina) associated with cerebellar calcification was encountered. The typical retinal angiomatosis appeared in only one eye and had been treated with radium. In 1 case a diagnosis of bilateral choroideremia was made. The central visual acuity in this case was normal, and the condition would have been unrecognized if a routine examination of the fundus had not been carried out.

In the second group, that of generalized diseases of the retina and choroid, 14 cases of retinitis pigmentosa were found. In 6 of these, central visual acuity was normal, and the condition probably would not have been diagnosed without routine ophthalmoscopic examination. One case of retinitis pigmentosa was unusual; a man aged 35 with perception of only light and motion in each eye was observed to have secondary choroideremia, severe chorioretinal atrophy due to retinitis pigmentosa of many years' duration. Both fundi were nearly white throughout except in the central region, where a few patches of recognizable choroid were present. Some pigment also occurred in the periphery. Two other cases of interesting conditions were noted in this group. One case was that of proved congenital syphilis in which typical "salt and pepper" fundi were seen, together with eighth nerve deafness and Hutchinson teeth but without interstitial keratitis. In the other case, an unusual fundus was seen; one eye had been penetrated by a fragment of an exploding dynamite cap. Temporally, near the optic nerve was a small piece of metallic copper surrounded by a large region of chorioretinitis, which also involved the macula. This lesion was of recent occurrence, and no lenticular changes had taken place.

The third group consisted of 97 cases of disease of the retina and choroid involving the central region. In 50 of these cases there was a definite history of trauma to one eye followed by loss of vision; in each of these cases severe disorganization of the central region was noted. These atrophic, usually heavily pigmented, lesions ordinarily showed no other retinal involvement. In 24 other cases there was a somewhat similar picture not associated with any history of trauma. Monocular central solar retinopathy (eclipse blindness) was noted in 11 cases. Visual acuity in these cases varied from 20/25 to 20/200. In each case the patient gave a history of viewing the sun during an eclipse in childhood, and in each instance the typical "punched-out," occasionally slightly pigmented, central retinal lesion was noted.

In 18 of the 38 cases of retinal detachment and allied conditions, there was a history of trauma, and a retinal tear could be found. In 5 cases these criteria were lacking, and the condition was classified as "idiopathic." Six cases of successful operative repair of retinal detachment were found. The longest period of such a reattachment was six years, and the shortest, one and a half years. Only 1 case of an unsuccessful attempt at operative repair was seen. An unusual condition closely related to retinal detachment was an easily seen, congenital nonattachment of the retina associated with monocular microphthalmos. The inner surface of the retina presented a funnel-shaped surface and was entirely smooth.

In the last group, that of myopic abnormalities, it is of note that in 9 of the 19 cases of chorioretinitis the associated high myopia was unilateral.

Monocular Loss of Vision.—A total of 2,932 cases of monocular loss of vision due to amblyopia (defined previously as corrected vision below 20/40), trauma or disease were seen in this series (4.9 per cent). In 836 of this number the loss was the direct result of trauma, whereas in 2,096 cases it was of nontraumatic origin (tables 6 and 7).

TABLE 6.—*Incidence of Nontraumatic Monocular Loss of Vision in a Series of 60,000 Selectees*

	Total No.	Ratio
Amblyopia without strabismus	855	1:70
Amblyopia with esotropia	770	1:78
Amblyopia with exotropia	295	1:203
Myopia, unilateral, high	48	1:1,250
Congenital cataract	44	1:1,360
Central chorioretinitis	24	1:2,500
Optic nerve atrophy, nontraumatic	20	1:3,000
Cataract, secondary	18	1:3,330
Glaucoma, primary and secondary	9	1:6,660
Retinal detachment, "idiopathic"	6	1:10,000
Coats's disease, active	2	1:30,000
Loss of one eye from ophthalmia neonatorum	2	1:30,000
Other conditions *	3	
	2,096	1:29

* One case each of active Eales's disease, van Hippel-Lindau disease and recurrent hemorrhages in the vitreous.

TABLE 7.—*Incidence of Post-Traumatic Monocular Loss of Vision in a Series of 60,000 Selectees*

	Total No.	Ratio
Traumatic loss of one eye	469	1:128
Traumatic cataract	109	1:550
Corneal scar, visual acuity below 20/40	71	1:845
Post-traumatic central chorioretinitis	50	1:1,200
Aphakia, operative and post-traumatic	49	1:1,224
Optic nerve atrophy, post-traumatic	25	1:2,400
Retinal detachment, post-traumatic	19	1:3,160
Post-traumatic dislocation of lens	12	1:5,000
Solar retinopathy	11	1:5,450
Retinitis proliferans, traumatic	6	1:10,000
Healed choroidal rupture	4	1:15,000
Post-traumatic retinopathy	4	1:15,000
Post-traumatic hemorrhage in vitreous	4	1:15,000
Other conditions *	3	
	836	1:72

* One case each of chorioretinitis due to metallic copper, loss of one eye following operative correction of strabismus and amblyopia ex anopsia with exotropia following extensive orbital scarring in infancy.

The 469 instances of "post-traumatic loss of one eye" represented a multiplicity of pathologic lesions. This term was used to include phthisis bulbi, any other involuntary process, extensive corneal leukoma and post-traumatic removal of one eye.

Post-Traumatic Conditions Without Visual Loss.—Sequelae of trauma were noted in 38 cases in which the corrected visual acuity remained 20/40 or better. In 21 of these cases eccentric corneal scars due to healed lacerations of the cornea were found. Seven cases of post-traumatic iridodialysis were seen in which no other abnormality was present. Anterior synechias were encountered in 6 cases. One unusual case was that of an old limbal laceration of the cornea with almost complete avulsion of the iris, resulting in post-traumatic aniridia. The remaining 3 cases comprised 1 case each of post-traumatic iridectomy and bilateral burns of the cornea due to lye and the interesting case of post-traumatic coloboma of the lens and iris previously described.

COMMENT

An interesting problem in ophthalmology concerns the association of so-called myopic chorioretinitis with high degrees of myopia. The precise etiologic factors involved in the production of the chorioretinitis are not known, and I believe the correct term should be "chorioretinitis of undetermined cause associated with myopia," although the shorter term is used here for convenience. Analysis of the 60,000 cases in this series indicates that a definite relation between these two conditions exists. Myopic chorioretinitis was found to occur frequently with unilateral high myopia; in 9 (19 per cent) of the 48 cases of unilateral high myopia this complication was present. In 9 (2.5 per cent) of the 362 cases of bilateral high myopia chorioretinitis was associated. In this series, therefore, chorioretinitis was associated with unilateral high myopia eight times as frequently as with bilateral high myopia. Not included is 1 case of unilateral myopic chorioretinitis associated with unilateral myopia of only 3 D. It is interesting to speculate as to whether the chorioretinitis associated with unilateral high myopia is primary or secondary. This question could be decided only by repeated examinations in such cases over a period of many years. Further, in conjunction with bilateral high myopia chorioretinitis of undetermined cause occurred more frequently than in otherwise normal eyes. As previously shown, in 2.5 per cent of the cases of high myopia chorioretinitis was associated. Exclusive of all cases of defects due to trauma, in the entire series of 60,000 cases there were only 52 cases (0.09 per cent) of chorioretinitis of undetermined cause as compared with the incidence with myopia. Thus, it appears that chorioretinitis of undetermined cause is associated twenty-eight times as frequently with high myopia as with eyes which are not myopic.

It is of note that in 18 of the 23 cases of uncomplicated retinal detachment retinal tears were present. In each of these cases there was a definite history of trauma, and careful ophthal-

moscopic examination with full cycloplegia revealed the hole. In several of the remaining 5 cases a history of trauma was elicited, but no tear could be discerned. In none of these cases of "idiopathic detachment" was the detachment secondary to subretinal tumor, as tested by transillumination of the globe. Seven cases of operative reattachment of the detached retina were noted. In all but 1 case the result was successful, with visual acuity in the various cases ranging from 20/100 to 20/20. In the single case of an unsuccessful attempt at operative reattachment, I was unable to find any evidence of a retinal tear, although thermal chorioretinitis was present, as it was also in the cases in which operation was successful.

Analysis of the results of ophthalmologic examinations in these cases reveals one finding of great practical importance from both the future military and the economic standpoint and affords evidence of the need for more effective preventive ophthalmologic practices. A total of 2,932 cases of monocular blindness or partial loss of visual acuity were found; this represents 4.9 per cent of the men in the entire series, or 1 out of each 20 examined. Further, this one condition, loss of vision of one eye, was by far the most common of any found in this series of 60,000 cases, since of the 5,712 cases of ocular abnormalities of all varieties, the 2,932 instances of monocular visual loss comprised more than half, or 51 per cent.

Extension of these figures to the number of men of military age of this nation indicates that of each million men, 49,000 are handicapped by poor vision in one eye. These men are less effective not only as members of the armed forces in time of war, but as members of society in time of peace. This situation is the more unfortunate since of these 2,932 cases of monocular visual loss, 94 per cent may be considered as representing preventible types. Cases of posttraumatic monocular blindness, 836 in number, comprised 28 per cent. In all these cases the blindness may be considered as preventible; in many cases it was caused by an industrial or occupational accident, and in others, by injury received in childhood from firecrackers, dynamite caps or other dangerous objects. Amblyopia was the type of poor vision found in 1,920 cases —in 855 cases without strabismus, in 770 cases with convergent strabismus and in 295 cases with divergent strabismus. Experience has shown that the diagnosis of amblyopia can be made in early childhood and, in nearly all cases, can be remedied by proper ophthalmologic measures, such as occlusion, refraction, orthoptic training and operative intervention. These 1,920 cases, together with 2 instances of ophthalmia neonatorum, form 66 per cent of all the cases of monocular visual loss. Thus, theoretically, only the remaining 6 per cent, or 174 cases, may be considered as instances of nonpreventible blindness.

Suitable preventive ophthalmologic measures should be taken in order to lower the percentage of men of military age handicapped by poor vision in one eye. The important factors to be considered in any such program are two: First, measures should be taken in order to reduce the incidence of post-traumatic monocular blindness. The existing educational and preventive program directed toward the prevention of industrial and occupational accidents should be expanded and broadened, and further efforts should be made to eliminate such ocular injuries as occur in childhood. Second, since amblyopia is responsible for 66 per cent of all monocular poor vision, particular efforts should be extended in order to reduce the incidence of this condition. Amblyopia can be remedied only in early childhood; therefore the diagnosis must be established at an early age. This could best be accomplished by routine ophthalmologic examination of each preschool child, followed by indicated ophthalmologic treatment. Great difficulties are inherent in any such program. However, the elimination of preventible monocular visual loss should be a goal of all organizations and persons interested in the conservation of vision.

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SYNDROME OF NONSYPHILITIC INTERSTITIAL KERATITIS AND VESTIBULOAUDITORY SYMPTOMS

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The purpose of this communication is to describe a clinical syndrome that, to my knowledge, is not generally recognized. I have been able to find only 1 instance of it previously reported in the literature.[1] The present report presents 4 cases. The syndrome consists of an interstitial keratitis associated with vertigo, tinnitus and usually profound deafness. The interstitial keratitis differs in its course and manifestations from that seen with congenital syphilis and occurs in persons in whom there are no signs or symptoms of syphilis. The cause of the syndrome is at present unknown.

The case previously reported[1] was that of a man aged 26 whose initial complaints were photophobia, epiphora, pain and redness of the eyes. Examination revealed that these were due to a symmetric interstitial keratitis. Two months after the onset of ocular symptoms there developed severe vertigo, nausea, ringing in the ears, deafness, rotary nystagmus and sweating on one side of the body. Wassermann tests on the blood and the spinal fluid gave negative reactions. The course is described as having been intermittent. Seventeen months after the onset a bilateral cervical ganglionectomy was done on the assumption that the disease was a vasomotor disturbance. During the subsequent year that the patient was observed mild attacks of vertigo continued, but the eyes cleared up entirely and there was distinct improvement in hearing.

The 4 patients whose cases are here reported were all seen by me within one year. They were not selected from a larger series of patients with interstitial keratitis; during the same period only 1 patient with active syphilitic interstital keratitis was observed.

REPORT OF CASES

CASE 1.—*History.*—E. C., a single, American-born Italian woman aged 22, has been under observation for six months. She is the youngest of 4 siblings, 3 of whom are reported to be in good general health. The first sibling died when 1½ years old, of "flu," during an epidemic of influenza. Both parents were living and well. The patient stated she had always been well except for "anemia" (treated by injections of sodium cacodylate), slight loss of weight in the past few years and one or two colds each winter. The last cold was three months prior to onset of the present illness.

Present Illness.—The onset was six months prior to the time of writing and was characterized by pain in the eyes, redness of the eyes, reduction in vision and photophobia. The symptoms began in the left eye but were followed within a few days by similar disturbances in the right eye. One week after onset of the ocular symptoms vertigo and noted diminution in hearing developed. The vertigo was described as having been severe and having produced the sensation of rotation of the room. Because of this vertigo the patient was bedridden for the first one and one-half months of the present illness. The vertigo was accompanied with a continual "roaring and sizzling in the ears" and with deafness. The patient was not taking salicylates or other medicament at the time the ocular complaint, vertigo and deafness began, but she subsequently took 40 grains (2.6 Gm.) of acetylsalicylic acid per day for several weeks.

During the first four months of the present illness the deafness gradually increased and the vertigo subsided. The ocular symptoms remained approximately the same as at the onset, but the patient observed that they, as well as the deafness, varied from day to day, being worse, she believed, in damp weather.

Examination was made four months after onset of the present illness.

Physical Examination.—Except for a large liver (not confirmed roentgenographically) the examination revealed nothing abnormal. There were no stigmas of congenital syphilis.

Ophthalmologic Examination.—Right Eye: Vision was 20/70. There were mild ciliary injection and moderate tenderness of the globe. Tension was normal to palpation. Yellowish white opacities were scattered throughout the deep portions of the cornea. With the slit lamp these opacities appeared granular and resembled an infiltrate. They were arranged in ill defined foci, approximately 0.5 mm. in diameter, and some were confluent. They did not extend appreciably into the anterior half of the stroma, and the surface of the cornea was smooth. There were no folds of the posterior surface of the cornea. The endothelium was abnormally pitted; but the pitting was much less than that seen in endothelial dystrophy, and the normal endothelial mosaic could be well seen between the pits. There were no precipitates on the posterior surface of the cornea, and the anterior chamber contained only 5 to 8 floating "cells" per low power field. The pupil was dilated from previous use of a mydriatic. The iris appeared normal and showed no synechia. The fundus was easily seen and appeared normal.

Left Eye: Vision was 20/200. The findings in this eye were indistinguishable from those in the other eye except that two "mutton fat" precipitates were present

From the Howe Laboratory of Ophthalmology, Harvard Medical School, and the Massachusetts Eye and Ear Infirmary.

1. Mogan, R. F., and Baumgartner, C. J.: Ménière's Disease Complicated by Recurrent Interstitial Keratitis: Excellent Results Following Cervical Ganglionectomy, West. J. Surg. **42**:628, 1934.

on the posterior surface of the cornea and two to three isolated vascular loops could be seen extending 1 to 2 mm. into the cornea.

Examination of the Ears, Nose and Throat.—Tests for bone conduction indicated extensive loss of cochlear function in both ears. No vestibular response was obtained on irrigation of either ear for twenty seconds with water at temperatures of 45 and 60 F. On irrigation for twenty-five seconds there was a fine nystagmus, which came on sixty seconds after termination of the irrigation of the right ear and fifty seconds after irrigation of the left ear. No nystagmus occurred after rotation in a Bárány chair ten times in twenty seconds, and minimal nystagmus appeared with rotation fifteen times in twenty seconds. These tests were interpreted as indicating pronounced hypoactive vestibular function on both sides.

Neurologic Examination.—The results were entirely negative except for the bilateral and symmetric involvement of the eighth nerves. Lumbar puncture showed normal dynamics of the spinal fluid.

Laboratory Data.—Urinalysis: The reactions for albumin and sugar were negative.

Blood: Count and smear: The first sample showed 5,050,000 red cells, 93 per cent hemoglobin, and 12,400 white cells, with 77 polymorphonuclear leukocytes, 24 lymphocytes, 2 mononuclears, 1 basophil and 4 eosinophils. The second sample showed 16,300 white cells, with 72 polymorphonuclear leukocytes, 18 lymphocytes, 4 mononuclears and 6 eosinophils.

Serologic tests: The Wassermann test gave a negative reaction on two occasions. The Hinton test (in dilution) gave a negative reaction.

Chemical constituents: Determination of the chemical constituents of the blood revealed 24 mg. of nonprotein nitrogen, 192 mg. of cholesterol, 3.9 mg. of phosphate, 1.3 units of phosphatase, 7.68 Gm. of protein, 5.61 Gm. of albumin and 2.07 Gm. of globulin per hundred cubic centimeters of blood. The albumin: globulin ratio was 2.7. The prothrombin time was twenty-six seconds.

Cerebrospinal Fluid: The cell count was zero. The protein measured 36 mg. and the sugar 72 mg. per hundred cubic centimeters; the colloidal gold curve was 0000110000, and the Wassermann reaction was negative. Culture yielded no pathogenic organisms.

Other Tests: The sulfobromophthalein sodium test revealed retention of 7 per cent (normal).

Analysis of the stool showed no cysts (ameba).

The tuberculin test gave a negative reaction in a dilution of 1 : 100,000.

Roentgenographic studies showed that the spleen and liver were of normal size, both mastoids were normal and the chest was clear.

Cultures of material from the conjunctival sac of each eye yielded no growth. Culture of secretions from the nose yielded coagulase-negative Staphylococcus albus.

Course of Illness.—The foregoing examinations were made approximately four months after the onset of the disease. The patient has now been followed two months longer. There has been no over-all change in the status of the eyes, although considerable variation has been observed in the corneal infiltrates, characterized by clearing in one region and their appearance in another. The ocular signs and symptoms were worse on some days than on others (possibly related to dampness), and varied in severity from one eye to the other. At no time has there been anything but a mild intraocular reaction, and the corneal vascularization remains insignificant. The deafness has slowly increased, showing changes from time to time but not apparently varying with the ocular symptoms. With the increasing deafness, the vertigo has almost completely disappeared, and the tinnitus is less. The patient has been continously afebrile.[1a]

CASE 2.—H. C., an American-born Greek milliner, aged 20, had been under observation for eight months. She was the third of 4 siblings. All the other siblings were well, and both parents were living and well. The Wassermann tests on both parents gave negative reactions. There was no history of deafness or other chronic disease in the family. The patient had always been well until the present illness.

The present illness began nine and one-half months prior to this report with pronounced photophobia, lacrimation, redness of the eyes and blurring of vision. Two weeks after onset of the ocular complaints there developed pronounced dizziness with apparent rotation of objects. This vertigo was intense at the onset, improved one week later but subsequently became severe again. It was accompanied by vomiting. During the initial two months of the illness there was said to have been aching of the left ear, and a tap of the ear was made, without, however, any discharge being obtained. A pronounced buzzing in both ears developed during the first few weeks of the illness. The patient was first examined six weeks after onset of the ocular complaint.

Physical Examination.—Inspection revealed nothing abnormal except the changes noted later. No stigmas of congenital syphilis were seen.

Neurologic Examination.—Rotary nystagmus was present with the eyes in the primary position, with the fast phase in the clockwise direction. This nystagmus was accentuated on the patient's looking to the left. There was constant nystagmus on her looking to the right and also downward. On her looking upward, there was an oblique nystagmus with a slight vertical component. The rest of the neurologic examination revealed nothing abnormal except for the deafness, but the patient was unable to stand up because of the extreme vertigo. Lumbar puncture showed normal fluid dynamics.

Ophthalmologic Examination.—Right Eye: Vision was 20/70. There were moderate ciliary redness and deep interstitial opacities of the cornea. Many fine deposits were present on the posterior surface of the cornea and many cells in the anterior chamber. The surface of the cornea was smooth and lustrous. There was no "take" with fluorescein stain.

Left Eye: Vision was 20/70. The eye was white and quiet. Few cells were noted in the anterior chamber, and a few mutton fat deposits occurred on the posterior surface of the cornea centrally, with a faint opacity of the deep stroma in one quadrant.

Examination of the Ears, Nose and Throat.—There were a scar on the left ear drum and deafness. No response was obtained on irrigation of the ears with water at temperatures of 68 and 40 F. respectively. Bone conduction was poor.

Laboratory Data.—Urinalysis (noncatheterized specimen): The urine was normal except for a 3 plus

1a. Since this report has gone to press, a unilateral cervical sympathetic ganglionectomy has been done, and the patient has been observed three months. No improvement in auditory or ocular symptoms has been noted during this time.

reaction for albumin, with white blood cells and epithelial cells on one of three occasions.

Blood: Count and smear: The first sample showed 18,500 white cells, with 63 polymorphonuclear leukocytes, 2 large lymphocytes, 26 small lymphocytes, 8 mononuclears and 1 eosinophil. The second sample showed 4,500,000 red cells and 12,800 white cells, and the third sample, 4,040,000 red cells; 86 per cent hemoglobin, and 13,700 white cells, with 76 polymorphonuclear leukocytes, 2 large lymphocytes, 14 small lymphocytes and 8 mononuclears.

Serologic tests: The Hinton test gave a negative reaction on four occasions, including once in dilution.

Cerebrospinal Fluid: The cell count was zero. The protein measured 28 mg. and the sugar 63 mg. per hundred cubic centimeters; the colloidal gold curve was 0000000000, and the Wasserman reaction was negative.

Tuberculin Test: The reaction was questionably positive in a 1:1,000 dilution.

Roentgenographic Study: Roentgenograms of the skull, the mastoids and the chest revealed nothing abnormal.

Cultures: Cultures of material from the conjunctival sac revealed coagulase-positive hemolytic Staphylococcus aureus.

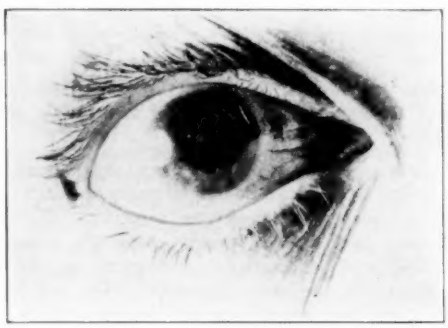

Fig. 1.—Right eye in case 2, showing patchy distribution of infiltrates in the cornea. The picture was taken six months after onset of the disease.

Course of Illness.—The foregoing examinations were made approximately six weeks after the onset. The nystagmus ceased soon after the patient came under observation, but the deafness progressed and the vertigo continued. The condition of the eyes showed considerable variability on examination at intervals of several days, being worse, according to the patient, in damp weather. Eight months after onset the patient was readmitted to the hospital for further study. The results of examination at that time were as follows:

Ophthalmologic Examination.—Right Eye: Vision was 20/70 and was not improved with the pinhole disk. There was mild ciliary injection. The surface of the cornea was smooth, with no epithelial edema. The corneal stroma was not appreciably swollen. Scattered throughout the posterior half of the cornea were grayish white, ill defined opacities (fig. 1). With the slit lamp these opacities now showed highly glistening qualities, in contrast to their dull appearance earlier. Loops of vessels now extended 4 to 5 mm. into the cornea and occupied a position immediately in front of the posterior surface. The posterior surface showed a few folds and ten to fifteen white precipitates, which were just large enough to be visible grossly. Examination of the anterior chamber was unsatisfactory because of the corneal opacity, but no cells were seen and the aqueous showed no outstanding flare. The pupil measured 4 mm. and showed no synechia. As far as could be determined through the cloudy cornea, the fundus was normal.

Left Eye: Vision was 20/100 and was unimproved with the pinhole disk. The eye was not injected. The findings were otherwise identical with those given for the right eye.

Otologic Examination.—The patient's deafness was practically complete; she could not hear the spoken voice. She heard the tuning fork with 1,024 vibrations per second in the left ear. No nystagmus was elicited with irrigation of either external auditory canal with 60 cc. of water at 38 F.

Additional Laboratory Data.—Blood: Count and smear: The hemoglobin concentration was 87 per cent; the red cells numbered 4,500,000 and the white cells 7,300, with 67 polymorphonuclear leukocytes, 25 lymphocytes, 4 mononuclears and 4 basophils.

Serologic studies: The Hinton, Kahn and Wassermann reactions were negative.

Chemical constituents: The cholesterol measured 200 mg. per hundred cubic centimeters.

Sedimentation rate: The rate was 5 mm. in twenty minutes and 22 mm. in one hour.

Dextrose tolerance test: The fasting level of the blood sugar was 129 mg. per hundred cubic centimeters; after one-half hour the sugar measured 197 mg., after one hour, 192 mg., after two hours, 177 mg., and after three hours, 161 mg. per hundred cubic centimeters of blood.

Additional Roentgenographic Data: Barium sulfate study of the stomach showed nothing abnormal. The gallbladder was normal (oral Graham test, with iodophthalein sodium). Roentgenograms of the chest revealed no lesions. The pyelogram showed no pathologic condition.

CASE 3.—J. L., a single, American-born Italian woman, aged 30, had been under observation for ten months at the time of this report. The patient was the fourth of 11 siblings. One died in infancy, and 1 was killed in military service. The others were living and well. Both parents were living and well, and Wassermann tests on both parents gave negative reactions. The history was difficult to obtain because of the patient's complete deafness and inability to read written questions. She apparently had had "ptomaine poisoning" just prior to the present illness but believed that she had been well before the onset of auditory and visual symptoms.

Present Illness.—The onset was seventeen months prior to the time of writing with deafness in the left ear associated with true vertigo (apparent rotation of the room), nausea and "buzzing in the ears." This was followed within two months by deafness in the right ear. At some time during the first few months of the present illness the patient complained of the eyes being irritated. There was no history of drug ingestion, infection or trauma. There had been no discharge, chills, fever or stiff neck. The vertigo decreased, but dizzy spells continued up to the time of the first examination. The deafness progressed and became complete in both ears. There was no family history of deafness or other chronic disease. The patient was first examined seven months after onset of the present illness, when she was admitted to the hospital with the tentative diagnosis of Ménière's disease.

Physical Examination.—Examination revealed nothing abnormal except for the bilateral nerve type of deafness and one abscessed tooth, which was removed. There was no saddle nose, notched teeth, periostitis or other evidence of congenital syphilis.

Neurologic Examination.—The findings were negative except for the deafness. Lumbar puncture showed normal fluid dynamics.

Ophthalmologic Examination.—Deep interstitial opacities which were characteristically patchy and associated with moderate ciliary injection were present bilaterally. There was no vascularization of the cornea and no posterior synechia. The pupils dilated well with atropine. There were pronounced photophobia and lacrimation, making a detailed study of the eyes difficult.

Examination of the Ears, Nose and Throat.—The diagnosis was "profound bilateral nerve deafness, with no residual hearing in the speech range." There was no response with massive cold caloric and Bárány turning tests.

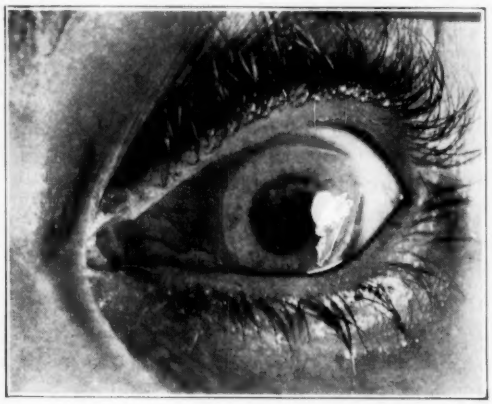

Fig. 2.—Left eye in case 3, showing infiltrates and some vascularization. The picture was taken ten months after onset of the disease.

Laboratory Data.—Blood: Count and smear: The first sample showed 10,800 white cells and 85 per cent hemoglobin; the second sample, 62 polymorphonuclear leukocytes, 22 small lymphocytes, 11 mononuclears and 5 eosinophils.

Serologic tests: The Wassermann reaction was negative on two occasions; the Hinton reaction was negative in three tests, including once in dilution.

Chemical constituents: The nonprotein nitrogen measured 22.5 mg.; the sugar, 87 mg., and the calcium, 9.5 mg. per hundred cubic centimeters.

Sedimentation rate: The sedimentation rate was 0.2 mm. a minute.

Urinalysis: The reactions for albumin and sugar were negative.

Cerebrospinal Fluid: The cell count revealed 1 polymorphonuclear leukocyte and 3 lymphocytes per cubic millimeter. The protein measured 25 mg. and the sugar 62 mg. per hundred cubic centimeters. The colloidal gold curve was 0001110000; the Wassermann reaction was negative, and culture yielded no growth.

Roentgenographic Study: Both mastoids were normal. The sinuses were clear except for a cyst in the outer wall of the right antrum. The chest was clear. The lower right first bicuspid was abscessed.

Culture: Culture of material from the conjunctival sac of each eye yielded no growth.

Course of Illness.—The foregoing examinations were made approximately seven months after the onset of the disease. The patient has been followed ten months longer, and during this time she has shown intermittent exacerbations of the ocular condition, with remissions in which, although the corneal infiltrate persists, the eyes are entirely white and quiet for several weeks at a time. During the exacerbations there were pronounced photophobia and lacrimation and an increase in the patchy infiltration of the deep corneal stroma. Only a few striae on the posterior surface of the cornea, no definite precipitates and only a mild intraocular reaction were present. The two eyes did not always show exacerbations at the same time. The remissions were characterized by a decrease in the ciliary injection and clearing of the corneal infiltrates, but at no time did the patches totally disappear. There has been no appreciable swelling of the corneal stroma, but vascularization has increased so that deep vessels now extended 5 to 6 mm. toward the center of the cornea (fig. 2). The deafness has remained practically complete, and the tinnitus continues.

Case 4.—B. A., a Jewish physician, married, aged 35, has been under observation three months. The family history was without significance. Both parents were living and well. The only significant item in the personal history was mild exposure to lewisite (dichlorobetachlorovinylarsine), with temporary ocular symptoms, two years previously.[2] The present illness began four months prior to this report with tinnitus and temporary deafness. Examination at this time showed audiometric loss in the midzone and for high tones. Two weeks following the appearance of auditory symptoms the patient complained of photophobia, redness and reduction in vision of the right eye only. Examination was made one week later.

Ophthalmologic Examination.—Right Eye: There was mild ciliary injection. The surface of the cornea was smooth. There was no "take" with fluorescein stain. Several opacities were present in the deep corneal stroma; these were characteristically patchy and were situated chiefly in the pupillary area. The endothelium on the posterior surface of the cornea appeared abnormally boggy. There were a few folds of the posterior surface, and 10 to 30 "cells" per low power field, in the anterior chamber. The fundus was normal.

Left Eye: The eye was normal.

Physical Examination.—Examination revealed nothing abnormal except for one abscessed tooth, which was subsequently removed, and chronic prostatitis.

Laboratory Data.—Blood: The first blood count revealed 5,400,000 red cells, 107 per cent hemoglobin, 11,300 white cells and 3 per cent eosinophils. The second count showed 10,400 white cells, with 6 per cent eosinophils.

The blood sedimentation rate was normal.

The Hinton and Kahn reactions were negative on two occasions.

Roentgenographic Study: the chest appeared normal.

Course.—The foregoing ophthalmologic examination was made approximately three weeks after onset of the auditory symptoms and one week after onset of the ocular symptoms. Within one week of the first ocular symptoms the eye cleared up entirely. One month later the patient again had transient tinnitus, this time unaccompanied by vertigo, and two days later a recurrence of the ocular symptoms. This again cleared up

2. Cogan, D. G.: Lewisite Burns of Eye, J. A. M. A. **122**:435 (June 12) 1943.

within a few days, and the abscessed tooth was removed. Within a few days after extraction of the tooth the patient again noted tinnitus, and photophobia developed. Examination at this time showed moderate injection of the sclera at the upper portion of the globe, but the cornea was clear. This attack also lasted only a few days. The patient's fourth, and most severe, attack occurred approximately two months after onset of the first symptoms. This attack was accompanied with mild, but definite, tinnitus in the right ear and, on one occasion, with vertigo. The right eye became tender and showed a nodular infiltration of the deep corneal stroma, similar to that seen when he was first examined. There were a few folds on the posterior surface of the cornea, and the aqueous humor was conspicuously colloidal. Again, the anterior surface of the cornea was smooth, and the infiltration was limited to the posterior half of the stroma. No abnormality of the iris was noted other than sluggishness to dilation with atropine. Visual acuity at this time was 20/30 in the right eye (with the pinhole disk) and 20/20 in the left eye. This attack was again limited to the right eye and cleared up completely approximately one week after the onset. Another exacerbation occurred approximately one month later, but in the interim the patient had had bronchopneumonia, during which a variety of bacteria (staphylococci, streptococci and pneumococci) were isolated from the throat. During this attack of pneumonia the patient had a "cold sore" in the nose, but tinnitus and ocular symptoms did not recur. Approximately two weeks after the attack of bronchopneumonia the patient complained of fairly severe ringing in the right ear, noticed especially on his placing the right ear to the pillow, and two days later he complained of tenderness in the right eye and reduced vision. Again, the right pupil required more than the usual amount of atropine to keep it dilated. Examination showed diffuse infiltration in the posterior half of the cornea, several localized deep foci and prominent folds on the posterior surface of the cornea. No precipitates were present. The intraocular pressure was normal. This attack again completely subsided, with disappearance of the corneal opacities within one week.

Résumé of Cases.—The clinical findings in cases 1, 2 and 3 were practically identical. All the patients were young women whose presenting complaints were severe vertigo, tinnitus, progressive bilateral deafness, pain in both eyes, ciliary injection, photophobia and somewhat reduced vision. Examination showed nerve type deafness with absence of labyrinthine function, a deep keratitis of both eyes characterized by patchy infiltration of the deep corneal stroma, little reaction in the anterior chamber and no apparent abnormality of the iris. The vertigo was sufficiently severe to confine the patient to bed for several weeks. The onset of vestibuloauditory symptoms and of ocular symptoms occurred within a few weeks of each other, the former occurring first in 2 cases and the latter in 1 case. The course of the illness in all cases was characteristically chronic. The vertigo diminished several weeks after the onset; in 2 cases the deafness became complete and the deafness in the case in which the patient has been under observation only two months at the time of writing is becoming progressively worse. The ocular signs have continued without substantial change for the entire period of observation (two months in case 1, eight months in case 2 and ten months in case 3) but have shown appreciable variation from day to day. The only consistent abnormality on systemic examination was an elevated white blood cell count. In 2 of the 3 cases there was mild eosinophilia (maximum 6 per cent). On the negative side, no evidence of syphilis could be obtained from the histories, the physical examination or repeated serologic tests in any of the cases.

Case 4 differed from the other 3 cases in that the patient was a man, the vestibuloauditory symptoms were relatively mild, with only temporary deafness, and the keratitis was limited to one eye and showed complete remission in the interval between attacks. However, in this case, like the others, there was unmistakable association of vestibuloauditory and ocular symptoms; the type of keratitis was the same, although less severe, and examination of the blood showed an increased white cell count and mild eosinophilia. Similarly, the process has continued over a period of months. In this case and in 1 of the other 3 cases abscessed teeth were noted.

All the patients are under observation at present, and in none of them can the disease be said, as yet, to be in an inactive stage.

All the patients live in widely separated districts near Boston. None of them has traveled outside the United States within the past few years, and none of them has been in contact, so far as is known, with persons returning from foreign countries.

COMMENT

Bilateral interstitial keratitis occurs predominantly in patients with congenital syphilis. A recent survey of the cases of interstitial keratitis showed that in 84 per cent either a positive serologic reaction or other stigmas of congenital syphilis were present.[3] Then, too, the association of deafness is not uncommon in cases of syphilitic interstitial keratitis, being approximately 4 per cent for the age group with which I am concerned.[4] These facts, together with the well known unreliability of negative serologic reactions in cases of congenital syphilis, may make it impossible to rule out this diagnosis with certainty, but congenital syphilis appears to be unlikely in the present cases, for the following reasons: The family histories were entirely negative for syphilis; e. g., no stillbirths

3. Sagher, E.: Die nichtluische Keratitis parenchymatosa, Zentralbl. f. d. ges. Ophth. **34**:305, 1935.

4. Dalsgaard-Nielsen, E.: Correlation Between Syphilitic Interstitial Keratitis and Deafness, Acta ophth. **16**:635, 1938.

or unexplained deaths occurred in infancy. Serologic tests performed on the parents in 2 cases gave negative reactions. No stigmas of congenital syphilis were noted. Repeated serologic tests in all the cases, and analogous tests on the spinal fluid in the 3 cases in which they were made, gave consistently negative results. The symptoms and course of the disease in these cases were different from those characteristic of syphilis. In all 4 cases the vestibuloauditory symptoms began abruptly with vertigo, tinnitus and deafness, at the same time as, or within a few days or weeks of, the ocular symptoms, whereas when vestibuloauditory symptoms accompany syphilitic interstitial keratitis, there is usually deafness only, and this, coming on slowly, does not begin for months or years after the ocular signs. Furthermore, deafness with syphilitic interstitial keratis occurs in cases in which, unlike the present ones, there is a history of especially severe interstitial keratitis.[4] The typical ocular signs of syphilitic interstitial keratitis are also different from those seen in the present cases. The typical bilateral syphilitic interstitial keratitis begins abruptly in one eye, followed in a period varying from days to weeks by involvement of the other eye; the disease reaches its peak within a week or two and shows a diffuse ground-glass or opalescent opacity of the cornea, which, in the course of a few weeks, becomes vascularized and then improves. The corneal thickness is increased several times. Iridocyclitis is also present to a varying, but usually severe, degree. In the present cases, however, there was no abrupt inception of the ocular signs, and even after months the appearance of the cornea did not differ greatly from that at the onset. The corneal opacities were deep, yellowish white and nodular, appeared to be made up of infiltrate and showed little or none of the diffuse ground-glass or opalescent opacity that goes with the severe swelling of the cornea associated with the usual interstitial keratitis. At no time was the corneal opacity as pronounced as that seen with syphilitic interstitial keratitis; the vascularization was much less, and there was no appreciable iridocyclitis. The course in the present cases has been more persistent than that of interstitial keratitis of syphilitic origin and showed greater fluctuations. It is concluded, therefore, that the weight of evidence is against syphilis as the cause of this syndrome.

Similarly, the condition in these 4 cases does not resemble interstitial keratitis presumably due to tuberculosis, which is typically a unilateral process and is accompanied with scleritis and focal iridocyclitis. Nor is there any evidence of the other agents, such as mumps, influenza and herpes zoster, which, as noted in a recent review,[3] have been reported to cause interstitial keratitis. The etiologic agent is not apparent in the present cases, and the only lead at present is the increased white cell count and the slight eosinophilia. In the 1 case previously reported remarkable improvement followed cervical ganglionectomy, and it was inferred that the cause of the disease was a disturbance of the sympathetic fibers.[1]

SUMMARY AND CONCLUSIONS

Four patients with a syndrome of nonsyphilitic interstitial keratitis and certain vestibuloauditory symptoms were observed. The disease is characterized by the abrupt onset of vertigo, tinnitus and deafness, with pain in the eyes, ciliary injection and reduced vision. The vertigo subsides usually as total deafness supervenes. The ocular signs are characterized by a patchy infiltration of the deep corneal stroma with minimal intraocular reaction. The signs, symptoms and course of the disease differ from those of congenital syphilis, and in the 4 cases described reasonably thorough search for evidence of syphilis gave entirely negative results. The cause of the disease was not discovered.

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Clinical Notes

A SIMPLE TECHNIC FOR CORNEAL TRANSPLANTATION

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SAN FRANCISCO

The history of and indications for corneal transplantation have been well covered in the European literature by Filatov and Tudor Thomas and in the literature of this country by Castroviejo. Those particularly interested in this subject will find comprehensive information in Castroviejo's articles. However, my colleagues and I have the impression that many ophthalmic surgeons fear to do a corneal transplantation because the technic appears too com-

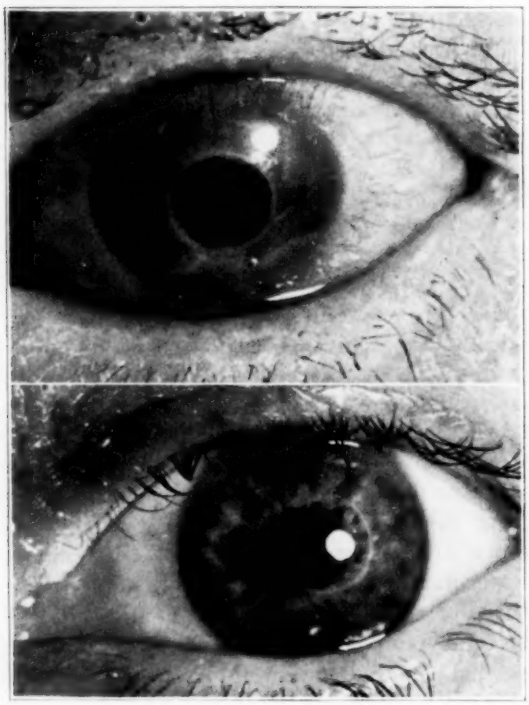

Fig. 1.—Photographs showing end result of corneal transplantation in 2 cases.

plicated to them, and we believe that many of the technics which have been described are of this nature, even though in experienced hands they undoubtedly have yielded satisfactory results. In 1940 A. S. Green and I [1] published an article describing a simplified technic for corneal transplantation. Since that time we have improved on this method, and here wish to describe the procedure, which can be easily followed by any ophthalmic surgeon.

From the Greens' Eye Hospital.

1. Green, A. S., and Green, M. I.: A Simplified Operation for Keratoplasty, Arch. Ophth. **24**:544-546 (Sept.) 1940.

In the past many of the failures in corneal transplantation have probably been due, first, to improper selection of cases and, second, to faulty technic. By "faulty technic" is meant a procedure in which too much manipulation is required both in preparing for the graft and in its

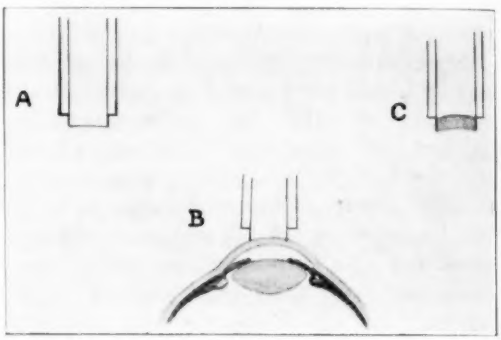

Fig. 2.—*A*, trephine blade with 1 mm. shoulder; *B*, superficial incision through epithelial layer of cornea of recipient's eye with trephine blade prior to staining with fluorescein; *C*, trephine blade containing the corneal disk in its lumen in readiness for transplanting.

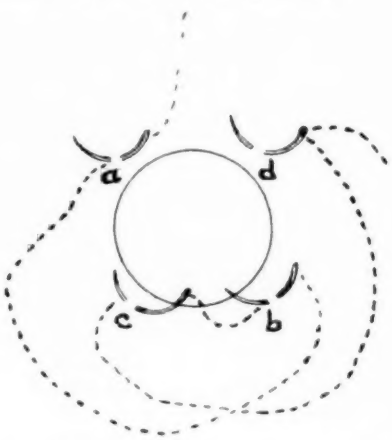

Fig. 3.—Diagram showing order of placing of the suture.

removal and transplantation. It is reasonable to assume that if there is a minimum of handling of the graft there is less risk that any of the layers of the cornea will be peeled off.

TECHNIC

The case having been selected according to well known indications, which have been repeatedly discussed in the literature on this subject, the following technic is used.

Green's automatic trephine is employed both for removal of the opaque corneal area from the recipient's eye and for obtaining the corneal graft. To remove the opaque corneal area from the recipient's eye a blade 4.1 mm. in diameter (fig. 2*A*) is used. This blade is designed so that it has a 1 mm. shoulder, the purpose of which is to prevent the blade from cutting deeper than the cornea, a provision to protect the lens from injury. The blade used for obtaining the graft is 4 mm. in diameter, and it also has a 1 mm. shoulder. The 4.1 mm. blade, detached from the trephine, is first placed over the cornea where the transplanting is to be done and is twirled between the thumb and the first finger a few times so as just to penetrate the epithelium (fig. 2*B*). A drop of fluorescein is then applied to the surface of the cornea so that the circular area is well outlined. The purpose of this procedure is to indicate where the suture is to be applied later.

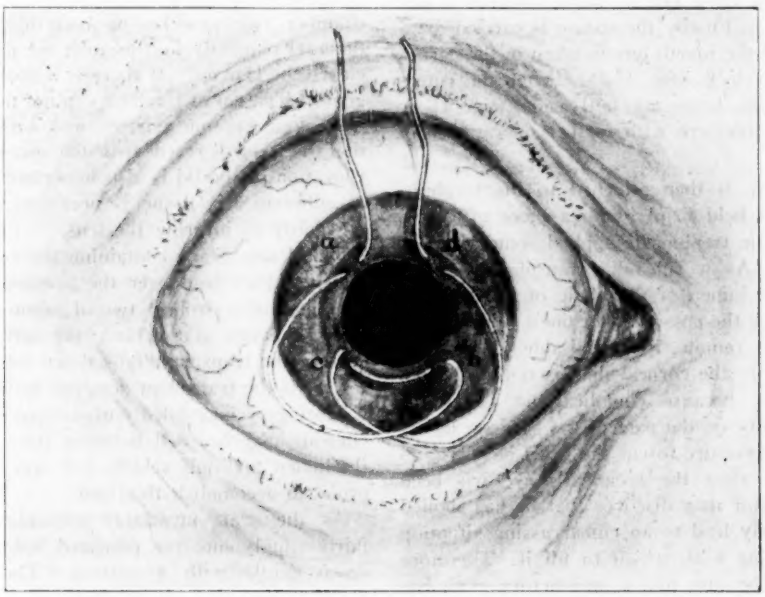

Fig. 4.—The suture has been placed and laid aside to permit excision of the corneal disk of the recipient's eye.

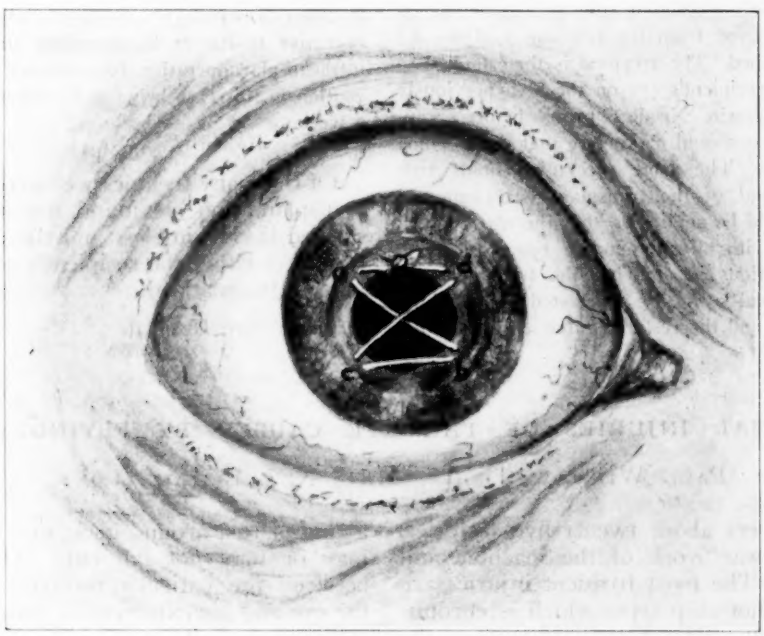

Fig. 5.—The suture drawn taut and tied above after insertion of the transplant.

An atraumatic needle threaded with fine silk is used for suturing. The suture is passed through the superficial layers of the cornea and always in the same direction, namely, from left to right of the surgeon, who stands at the head of the patient. Four bites are taken, in the following order, through the superficial

layers of the cornea several millimeters outside the circle outlined with the fluorescein. The first bite is taken between 10 and 11 o'clock (fig. 3, *a*). The suture is then carried downward diagonally, and a second bite is taken in the cornea, in the same direction, between 4 and 5 o'clock (fig. 3, *b*). The suture is then carried to the right, and a third bite is taken between 7 and 8 o'clock (fig. 3, *c*). Finally the suture is carried diagonally upward, and the fourth bite is taken in the cornea between 1 and 2 o'clock (fig. 3, *d*). After the suture has been applied the loops are laid aside (fig. 4) so that they will not interfere with further operative procedures.

The 4 mm. blade is then attached to the trephine. The donor's eye is held firmly with a piece of gauze, and as the automatic trephine is applied some pressure is exerted on it. As a rule the transplant remains securely within the lumen of the blade of the trephine (fig. 2 *C*). Although the possibility of one's being unable to obtain a graft is remote, it is advisable to have the graft available before the corneal disk is removed from the recipient's eye, because complications can arise, owing to overtimidity on the part of the surgeon in not applying sufficient pressure to cut the graft cleanly, and it is possible that after the recipient's eye has been prepared, the operator may discover that he has spoiled the graft, which may lead to an embarrassing situation —a hole and nothing with which to fill it. Therefore one should always be sure that a satisfactory graft has been cut before opening the anterior chamber of the recipient's eye.

The 4 mm. blade containing the transplant in its lumen is then removed from the trephine, and the 4.1 mm. blade is attached. The trephine is then applied to the cornea of the recipient's eye on the area previously outlined with fluorescein. Needless to say, before carrying out this step one should make sure that the trephine has been rewound. The same precaution holds true here as for removal of the transplant—sufficient and firm pressure should be applied so that the corneal disk comes out clean, with all surrounding tissue removed. If one is too cautious in applying the trephine, only about half the corneal layers are penetrated; the trephine must be reapplied, and the result is often a ragged edge to the wound. This may be responsible for some of the failures in corneal transplantation.

If the trephine has been applied with the correct degree of pressure, the corneal opening of the recipient's eye is clear and clean. If adhesions to the iris are present, they are excised. Another drop of solution of atropine sulfate, 1 per cent, is dropped into the anterior chamber (atropine having been instilled before operation). Frequently by this time the patient remarks how clearly he can see. If there is a prolapse of the iris, by gentle elevation of the lid speculum the anterior chamber may again become existent, and with careful manipulation the iris will recede from the opening in a few minutes. Elevation of the lid is also important whenever excision of adherent iris tissue is necessary, as it reduces the possibility of injuring the lens.

The 4 mm. blade containing the transplant within its lumen is then held over the prepared recipient corneal opening, and a drop or two of saline solution is instilled into the barrel of the blade through its upper opening, so that the transplant falls down into the bed prepared for it. If the transplant does not deliver readily, a small irrigating syringe filled with isotonic solution of sodium chloride may be used to force the graft gently out of the lumen, and only seldom is it necessary to use a blunt probe to accomplish this step.

As the graft invariably expands somewhat, it fits fairly snugly into the prepared bed and can be patted down gently with a spatula. The suture is drawn together and tied above at about 12 o'clock (fig. 5); another drop of solution of atropine is instilled, and the eye is closed. The upper lid is held down by a lid suture, as after a cataract operation. The immediate postoperative treatment is essentially the same as that of intracapsular operation for cataract, the principal precaution in this case being not to open the eye for about a week.

COMMENT

Of the many technics we have tried for corneal transplantation we found that the one just described is the simplest and the one in which the cornea of either the recipient's or the donor's eye is least traumatized.

Greens' Eye Hospital.

INDUSTRIAL INJURIES OF THE EYE CAUSED BY FLYING OBJECTS

PAUL WINSLOW TISHER, M.D., NEW BRITAIN, CONN.

This area covers about twenty-five factories, all engaged in war work of the machine and hardware type. The most frequent injuries are of the so-called hot chip type, which is encountered in grinding. The typical history is the slight sensation of something in the eye, which causes, usually, only momentary discomfort. Often, especially if there is an element of carelessness, the worker does not go to the nurse; or, if he does, she may fail to discern the foreign body. The worker goes home and three to four hours later begins to have pain in the involved eye. By that time the metallic particle has formed a ring of rust around itself, and the foreign body may or may not fall out. The time interval between the patient's receiving the particle in the eye and his experiencing pain and discomfort sufficient to call attention to it varies with the type of metal being used and his individual reaction. A small metallic foreign body can be carried in the cornea for a week or more with only slight discomfort. Many metallic foreign bodies will, on the second or third day, spontaneously extrude themselves from their corneal bed as a result of the associated infection. Most of these infections are what one might call endogenous,

or at least specific to the eye, because the average hot chip is sterile, due to its own heat on leaving the grinding wheel.

A corneal foreign body near the limbus is more painful than one nearer the center. This is unfortunate because, owing to the relative lack of pain caused by an object near the center, it may be allowed to remain long enough to produce infection. Even a slight scarring effect of an infected foreign body at the center of the cornea may cause considerable loss of vision. This fact is also especially significant should unskilled hands attempt to remove the object from the eye. The nearer the object to the center, the greater the possibility of loss of visual acuity.

The average, simple injury due to a foreign body of the so-called grinder type can be divided into three stages. In the first stage, in which the chip of steel or grinding wheel speck is seen within a few hours after its arrival on the cornea, the particle is usually removed with a sharp point. After-care is simple—an anesthetic or an antiseptic ointment of almost any kind will suffice. In the second stage, in which the chip or speck has been in the eye for twelve to twenty-four hours, the object is often hard to remove because the iron element has oxidized, with extension of a ring of ferric oxide stain into Bowman's membrane and the underlying stroma, which is contiguous to Bowman's membrane, there being no line of cleavage. The foreign body and the ring of stained stroma should be removed, for if left in place they will delay healing or may in time slough, extending the size of the ulcer crater unnecessarily. The third stage is that in which the foreign body is seen twenty-four to forty-eight hours or more after the injury. The foreign body itself may already have fallen away. The ring of rust is usually readily removed because the bacterial flora of the conjunctival sac sets up sufficient infection around the object to break down the corneal stroma, which I previously described as attached to the object. There, again, a sharp point is used to go completely to the base of the ulcer area and remove all infected debris. Some surgeons prefer to use a dental burr to cleanse completely the crater of the ulcer.

After cleansing, it is well to employ additional therapy. Badly infected craters can be cleansed by the application in about half-strength of a 3.5 per cent solution of iodine on a fine tip. The excess iodine can be neutralized with 4 per cent cocaine hydrochloride, with which it combines to form a cocaine iodate. This is then removed by irrigation. Application of merbromin on a point is also efficient, and takes much less effort. Of late, sulfadiazine powder has been applied directly to the ulcer crater after it has been cleansed. This can be combined with either of the procedures already described if the severity of the infection warrants. It seem that the period of discomfort is shorter, since the ulcer area is definitely cleaner. The sulfadiazine powder applied directly to the crater seems to be more effective than use of a sulfathiazole ointment. As a matter of comment, I have wondered whether the effect of the sulfathiazole ointment was not due as much to the ointment itself as to the sulfathiazole. The sulfadiazine powder is applied directly with slight pressure, a flat spatula or an old iris repositor being used. Loose sulfadiazine powder spilled in the conjunctival sac does not seem to be particularly beneficial except in cases of frank conjunctivitis. It is true perhaps that in the average case of a foreign body the eye will clear after simple removal of the object and ordinary first aid, but owing to wartime stress, the period of incapacity for the factory worker needs to be shortened as much as possible. This procedure may involve extra trouble, but experience has shown that the average patient is back to work much quicker because of it.

The question of whether to pad or patch the eye arises after removal of the object. We have practically ceased using the patch except in cases in which a large amount of corneal epithelium has been lost by the trauma. The patch looks unsightly and is uncomfortable, and so often, especially in the case of the average mill worker, there is present a low grade catarrhal conjunctivitis secondary to the dust in the factory. This will flare up if the eye is padded. The frequent application of an ointment containing mercury bichloride (1:3,000) will fill in the ulcer crater better and, at the same time, serve as sufficient therapy for the conjunctivitis. If iodine is used to cauterize an ulcer bed, mercurial ointments cannot be put in the eye immediately afterward. Also, there is usually a period of pain two hours after the treatment which must be controlled by use of anesthetics in the eye. Failure of the ulcer crater to heal well in a few days may be due to conjunctivitis. This reaction may be a flare-up of the patient's own conjunctivitis or may be secondary to dust or infectious matter brought in at the time of the original injury. The old-fashioned "silver scrub" treatment, with use of 1 or 2 per cent solution of silver nitrate on a cotton tip and gentle massage of the upper and lower conjunctival areas with the lids everted is still good treatment. The patient suffers a good deal less if the silver nitrate is neutralized by applying a cotton pack saturated with a solution of boric acid to the area treated for a few minutes before the lids are allowed to return to their normal position. If the reaction is still severe, it can be relieved by waiting about ten minutes and then irrigating the conjunctival sacs copiously with solution of boric acid. Irrigation of the tear ducts with any of the commonly used mild antiseptic solutions is helpful, as it clears the infection out of the tear sac and at the same

time probably feeds the antiseptic back to the cul-de-sac for a while after treatment.

Another frequent ocular injury in this area is a blow to the eye or to the adnexa or to the skull itself from a flying object, or even a part of a machine. As in all accident cases, vision is determined with and without glasses before treatment is started. Examination of the fundus should be thorough and atropine used freely if there is direct trauma to the eyeball, as this will often control low grade post-traumatic iritis. Blows to the head require just as thorough an examination of the fundus, with dilation of the pupils, to pick up retinal tears, retinal or choroidal detachments and macular damage in the form of edema or hemorrhage, or even the traumatic lesion known as a hole in the macula. These lesions of the retina may occur by direct or indirect trauma or by contrecoup. Commotio retinae (Berlin's traumatic edema) and rupture of the choroid, which is seen fairly frequently, are more apt to be due to direct trauma. I have seen several cases of such injuries, in which a high speed grinding wheel has literally exploded in a worker's face, thereby releasing various-sized fragments in all directions at high speed, owing to the terrific centrifugal force. Studies of the visual fields will often help in clarifying or substantiating visual findings or reveal damage not seen ophthalmoscopically. Damage to the optic nerve does not always manifest itself at the first examination. If there is reason to expect changes, it is well to advise a later check-up.

Intraocular foreign bodies present problems of their own, but it is of foremost importance not to miss the presence of such a body. It is amazing to observe how many times a patient may have an intraocular foreign body and not realize it, owing to the absence of pain or visual difficulty. On several occasions the patient has complained only that a drop of oil struck the eye, yet I have found chips of steel which have gone through the limbus, pierced the base of the iris, passed around the edge of the lens and lodged almost anywhere in the eye. This type of injury is most apt to occur when two metallic objects come together forcefully and a line of cleavage of the crystalline structure is created, which spalls a small piece of metal at high speed in almost any direction. These particles are usually sharply pointed, almost needle-like. They are sterile, due to the terrific heat created at the time and place of the spall. The procedure to be followed is governed largely by the ultimate location of the object, the degree of reaction and the time interval between the occurrence of the accident and observation by the physician.

Any injury of an eye is capable of destroying the sight of that eye and of the fellow eye. This axiom makes it imperative to keep good records for all patients treated. No patient should be treated until the visual acuity is taken, with or without glasses, as the case may be, and an examination of the fundus made, if possible. These recorded facts protect oneself and the patient, guard against malingering and aid in the determination of the amount of loss of vision and the extent of the liability that the employer may have to assume. As a matter of convenience I use a printed form in which the visual acuity is stated, together with a simple description of the injury, what was done and instructions to the factory nurse. This is sent back with the patient.

The ideal program would be to have every employee examined before beginning employment so as to have a definite visual record and a classification for the most efficient job placement. This would also serve as a basis for estimation of liability in case of accident.

99 West Main Street.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Conjunctiva

THE ENDOCRINE TREATMENT OF KERATOCONJUNCTIVITIS SICCA. J. J. FRIED and MAX A. GOLDZIEHER, Am. J. Ophth. **27:** 1003 (Sept.) 1944.

Fried and Goldzieher give the following summary:

"A case of keratoconjunctivitis sicca observed over a period of three years is reported. Treatment with the standard ophthalmologic methods was unsuccessful. Remarkable improvement, practically amounting to a cure, was obtained by administration of estrogens. A relapse not controlled by increased dosage of estrogen yielded to added treatment with progesterone.

"These observations confirm the belief that deficiency of sex hormones plays an important role in the pathogenesis of Sjögren's disease."

W. S. REESE.

Cornea and Sclera

CORNEAL VASCULARITY AS SIGN OF ARIBOFLAVINOSIS. J. G. SCOTT, J. Roy. Army M. Corps **82:** 133 (March) 1944.

Of 536 Europeans, 37 per cent, and of 1,700 Africans, 5 per cent, presented corneal vascularity. As judged by the presence of perlèche, cheilosis and glossitis, the Africans had twice as many cases of ariboflavinosis as did the Europeans. Corneal vascularity therefore cannot be taken as a guide to avitaminosis in the African. Of 136 Europeans who were examined with the slit lamp, 70 took a course of riboflavin treatments, while 50 acted as controls. This therapeutic test gave negative results. The degree of vascularity fluctuates with or without riboflavin therapy. Corneal vascularity cannot be accepted as a guide to avitaminosis in Europeans. All the Africans examined had a rim of pigment at the corneoscleral junction. It is possible that this rim explains the striking difference in African and European corneal vascularity.

J. A. M. A. (W. ZENTMAYER.)

General

THE INCIDENCE OF EYE DISEASE IN THE AUSTRALIAN IMPERIAL FORCES, MIDDLE EAST. J. BRUCE HAMILTON, Brit. J. Ophth. **28:** 383 (Aug.) 1944.

This survey deals with 3,638 patients seen during 1941-1942, with 5,650 diseased conditions classified under 226 headings. This gives a ratio of 1.55 diseases per patient. The figures and percentages for civilian and military diseases of the eye are arranged side by side in five tables. The data on certain diseases are grouped together in four tables. It appears that in wartime there is less ocular disease among military personnel than among civilians in peacetime. Certainly, there are fewer ocular injuries. The incidence of civilian injuries of the eye is 15.6 per cent, and the incidence of injuries in the army, 9.4 per cent. On the medical side, the incidences of iritis, keratitis, choroiditis and retinitis are also lower. Hamilton has not seen sympathetic ophthalmia in military practice despite the fact that he has had no facilities for slit lamp microscopy. Iridocyclitis is rare in the army.

W. ZENTMAYER.

Injuries

MANAGEMENT OF FOREIGN BODIES IN THE EYE. P. G. MOORE, Ohio State M. J. **40:** 26 (Jan.) 1944.

This is a general and comprehensive consideration of the management of foreign bodies in the eye and does not lend itself to abstract.

The subject is considered under the following headings: method of examination, instrumentation and anesthesia, observation of cases, disadvantage of bandaging and after-treatment. Special paragraphs deal with the removal of foreign bodies from the cornea and intraocular foreign bodies.

W. ZENTMAYER.

REMOVAL OF A NON-MAGNETIC FOREIGN BODY FROM THE VITREOUS. V. O'HEA-CUSSEN, Brit. J. Ophth. **28:** 296 (June) 1944.

While he was mining phosphates, the patient was struck in the left eye by a flying particle which caused immediate loss of sight. There was a small central perforation of the cornea with a stellate opacity in the posterior layers of the lens, preventing examination of the fundus. A roentgenogram revealed a foreign body in the vitreous. Eighteen days later the lenticular opacity had entirely disappeared. Observation showed extreme motility of the foreign body. About three weeks after the injury, immediately over the estimated position of the foreign body, two sutures of catgut with mounted needles were passed through the superficial layers of the sclera 2 mm. apart.

With the belly of a cataract knife, an incision was made and deepened until the choroid was

exposed. While vertical traction was made on the sutures, the incision was carried through the choroid and retina the full length of the scleral incision. The foreign body, which was easily removed by means of a narrow curet, proved to be a piece of stone. The author believes the technic employed reduced the loss of vitreous to a minimum. He points out that the magnification of a foreign body in the anterior layers of the vitreous is roughly 3 diameters.

W. ZENTMAYER.

THE LATE RESULTS OF REMOVAL OF INTRA-OCULAR FOREIGN BODIES WITH THE MAGNET. P. D. TREVOR-ROPER, Brit. J. Ophth. **28:** 361 (July) 1944.

The authors supply the following summary:

"The late results of 150 recent cases of removal of magnetic intra-ocular foreign bodies have been analyzed and the factors affecting the prognosis assayed. Uveal and lens damage are both of great importance in reducing the ultimate vision. The site of the entry wound is of moderate significance, those at the limbus and ciliary region having the worst outlook. Delay in dealing with the foreign body is not of much consequence.

"The lens was injured in two-thirds of the cases; of these a quarter lost the eye, but in a further 14 per cent, the cataract remained localized enough to allow reading vision (6/18 or better). Where the lens was uninjured the prognosis was fair, two-thirds of these cases retaining good vision.

"The posterior route and the Mellinger magnet have been very rarely used; reasons for this are offered.

"The strengths of the magnetic fields from the various pole-pieces have been established.

W. ZENTMAYER.

Lacrimal Apparatus

A SIMPLIFIED EXTERNAL DACRYOCYSTORHINOSTOMY. J. L. D. WILLIAMS and B. G. HILL, Brit. J. Ophth. **28:** 407 (Aug.) 1944.

The authors describe a simple method of keeping a graft from the lacrimal sac in position in external dacryocystorhinostomy which requires the use of no special instruments other than those provided in the equipment of a military hospital. Rubber tubing is introduced to do this. The article should be consulted for the details of the operation.

W. ZENTMAYER.

Neurology

OCULAR NEUROSIS. A. M. G. CAMPBELL and A. G. CROSS, Brit. J. Ophth. **28:** 394 (Aug.) 1944.

After examination of 500 consecutive patients with ocular neuroses attending a service ophthalmic clinic in wartime in the British Isles, the author estimates that the disturbance in 34 per cent was psychogenic rather than organic. Case histories are given to illustrate the influence of a psychiatric background, environment, ocular awareness, domestic stress, head injuries and flying. The clinical manifestations include blindness and defective vision, asthenopia, photophobia and excessive blinking, night blindness and diplopia. Malingering is considered rare. The cases described are seen primarily by the ophthalmologist, and it is desirable, if he is not a skilled psychiatrist, that they be referred for psychologic investigation of the underlying causes of the symptoms.

W. ZENTMAYER.

Ocular Muscles

PTOSIS — POSTTRAUMATIC AND HYSTERICAL. E. B. SPAETH, Am. J. Ophth. **27:** 687 (July) 1944.

Spaeth presents an unusual oculomotor condition following trauma. The diagnosis of hysteria was based on inconsistencies in the symptoms and neuroanatomic impossibilities. Time and subsequent observations verified this diagnosis. Up to the time of abrupt recovery the gross incongruities in the extraocular muscles could not be answered on an organic basis.

W. S. REESE.

THE CHOICE OF THE FIXATING EYE IN PARALYTIC AND NONPARALYTIC STRABISMUS. J. W. WHITE, Am. J. Ophth. **27:** 817 (Aug.) 1944.

In this article the author discusses different types of fixation and the type of surgical intervention required for some of these conditions.

W. S. REESE.

OPERATIONS ON ONE HUNDRED CASES OF CONVERGENT CONCOMITANT SQUINT. S. H. FAULKNER, E. SCULLY and E. E. CARTER, Brit. J. Ophth. **28:** 403 (Aug.) 1944.

The authors give the following summary:

"1. The result of operative treatment for convergent concomitant squint in 100 cases unsuitable for orthoptic treatment alone is described.

"2. Ninety-two of the cases were rendered approximately straight by operation and orthoptics.

"3. One patient considered to be a case of psychological squint was unimproved with repeated operation.

"4. Of the seven remaining relatively unsatisfactory cases, it is likely that most would have responded to further operation.

"5. Of 45 treatment cases with binocular vision at the angle of squint, 33 satisfied the conditions of cure according to the proposed standard of the British Orthoptic Association.

"6. Greater cooperation of the parents in allowing a further operation in cases with a residual angle and in bringing the children for post-operative orthoptic treatment would have reduced the number of patients classed as failures from the point of view of normal binocular vision."

W. ZENTMAYER.

Operations

THE HISTORY AND DEVELOPMENT OF THE IRIS-INCLUSION OPERATIONS. T. D. ALLEN, Am. J. Ophth. **27:** 964 (Sept.) 1944.

Allen gives the following summary of this interesting article:

"In this article an attempt is made to show the methods used by the early ophthalmologists to relieve suffering and postpone blindness; first, in the prescientific era from approximately 1800 to 1850; second, in the early scientific era from 1850 to 1900; and finally in the last 40 years.

"During the first period, diagnosis was very crude, medical treatment was very severe, and surgical treatment was done in an empiric manner.

"In the second period, as a result of more exact methods of examining the living eye, as well as the enucleated eye, there was an improvement in the technique. This was aided by an international interchange of opinions by the leaders in various countries. As a result of this certain opinions, which had been considered true, had to be questioned. Clinical observations improved in quality, and, from the second stage, gradually is evolving the third stage of more exact diagnosis and more logical treatment.

"Several operations such as the trephine and cyclodialysis have hardly been mentioned because in advocating them the authors have never suggested that iris be included in a scleral section; in fact, meticulous avoidance was impressed upon all who would attempt them."

W. S. REESE.

Orbit, Eyeball and Accessory Sinuses

THE EXOPHTHALMOS OF HYPERTHYROIDISM. J. H. MULVANY, Am. J. Ophth. **27:** 693 (July); 820 (Aug.) 1944.

The second part of the article deals with the differentiation with respect to the mechanism, pathology, symptoms and treatment of two varieties of exophthalmos.

In the concluding, or third, section of this article an extensive summary and bibliography are given, and the following conclusion is made.

"Concerning the exophthalmos of hyperthyroidism, the existence of a differentiation complete in respect to mechanism, pathology, symptomatology, and response to treatment suggests that two diseases are concerned instead of one, as has been the accepted opinion heretofore.

"The exophthalmos of thyrotoxicosis appears to develop and be maintained independently of hypophyseal control. It often bears some relationship to the severity of the disease and tends to show improvement after thyroidectomy. The thyrotropic hormone has never been found in increased quantities in the serum of any unquestionable instance.

"Thyrotropic exophthalmos, on the other hand, is undoubtedly of pituitary origin, being certainly associated with increased formation of thyrotropic hormone and possibly also of one or more sterones. Hyperthyroidism, an essential component of the condition at one stage or other, bears no more than a casual relation to the proptosis. The control of hyperthyroidism by thyroidectomy often leads to severe aggravation of the proptosis on account of the stimulus to increased secretory activity of the pituitary gland.

"Thyrotropic exophthalmos never develops into classical exopthalmic goiter; conversely, the latter is not associated with the progressive thyrotropic exophthalmos."

W. S. REESE.

ORBITAL CELLULITIS TREATED SUCCESSFULLY WITH PENICILLIN. H. O. SLOANE, J.A.M.A. **126:** 164 (Sept. 16) 1944.

The author supplies the following summary:

"In a case of orbital cellulitis of the left eye in a boy of 12 the cause was established to be sinusitis involving the left ethmoids and the maxillary antrum. Operation was contemplated both for the sinus condition and locally to establish drainage and relieve the inflammation and swelling of the orbital tissues. However, under the continued use of penicillin intravenously for a period of ten days the condition cleared up completely, so that it was unnecessary to operate. Sulfadiazine in fairly large doses was tried without affecting the disease in any way and was discontinued when penicillin was administered. Local treatment was limited to applications of hot magnesium sulfate solution continuously and instillation of atropine sulfate 1 per cent three times daily."

W. ZENTMAYER.

Pharmacology

CHOLINE ESTERS WITH MYDRIATIC AND CYCLOPLEGIC ACTION. K. C. SWAN and N. G. WHITE, Am. J. Ophth. **27:** 933 (Sept.) 1944.

Swan and White draw the following conclusions from this technical article:

"Balancing of the hydrophilic quaternary ammonium group in carbaminoylcholine (doryl) with hydrophobic carbon groups results in a reversal of its pharmacologic action on the intraocular muscles. Whereas carbamylcholine (doryl) produces miosis and cyclotonia, di-n-butyl-carbamylcholine produces mydriasis and

cycloplegia. Correlation of physical properties with the pharmacologic action of other new drugs synthesized by the authors indicates that the unique reversal of action of carbamylcholine seems dependent upon its conversion to a surface-active compound. The surface-active carbamylcholine derivatives have a potent peripheral antispasmodic action on the smooth muscles of the eye innervated by the parasympathetic nervous system; that is, the iris sphincter and ciliary muscles. The mydriatic and cycloplegic effects of other surface-active choline esters are considerably weaker.

"The surface-active carbamylcholine derivatives are chemically unrelated to previously known mydriatic and cycloplegic agents—for example, the atropine series—and, therefore, constitute a new class of drugs. For clinical purposes the sulfate appears to be the most satisfactory salt and dibutoline the most effective member of the new class. It is suggested that the new drugs may act as 'inhibitory analogues' of acetylcholine."

W. S. Reese.

Trachoma

Trachoma in London: The End of a Chapter. Arnold Sorsby, Brit. M. J. **2:** 220 (Aug. 12) 1944.

On May 10, 1944, the last five remaining children in one of the hospitals of the London County Council at White Oaks were discharged and the block was closed down. This indicates that trachoma in school children has been eliminated in London. In 1935 Sorsby gave an account of how trachoma came to be introduced among the children under the care of the Poor Law authorities in the first half of the last century and the many difficulties which arose in the handling of this serious condition. Nettleship and his wife, in 1872, at a temporary isolation school at Anerley, and Stephenson, in 1889, at Hanwell, demonstrated that trachoma could be stamped out by effective segregation and treatment. Notwithstanding, the recommendations of the committee were slowly accepted, and it was only in 1903 that two hospital schools, with a total capacity of 720, were opened. In 1918 one of these schools became superfluous, and that school was closed. To the remaining school, at White Oaks, it is interesting to note that in 1903 there were 292 admissions. From 1904 to 1913 there was a yearly average of 112 admissions; from 1914 to 1923 there were 29 admissions; from 1924 to 1933, 34 admissions, and from 1934 to 1943, 13 admissions. The decline in the number of admissions during the past ten years has been steady, until it was reduced to a final figure of 7. At the same time, trachoma is still not infrequent in London, as is obvious from the number of adult patients seen at the eye hospitals. Each case presents an individual and social problem, as well as a source of potential epidemic.

To show what can be accomplished by systematic and persistent effort, the experience in Glasgow in the treatment of trachoma in adults is interesting. In 1915 there were 112 new cases of trachoma, which number has gradually declined, until in 1943 there were only 3 new cases. In London there have been no systematic special provisions for the preschool child or the adult. In the light of the history of what has been achieved in Glasgow, it follows that statutory notification and the provision of adequate facilities for the energetic treatment of patients with trachoma should be established in London.

Arnold Knapp.

Tumors

I. Metastatic Carcinoma of the Choroid; II. General Metastasis From a Melanoma of the Abdominal Wall, with Paresis of the External-Rectus Muscle; III. Rubeosis Iridis, with Melanoma of the Choroid and Secondary Glaucoma. E. C. Ellett, Am. J. Ophth. **27:** 726 (July) 1944.

Ellett briefly discusses metastatic carcinoma of the eye and reports 2 interesting cases. He also reports a case of general metastasis from a melanoma of the abdominal wall with paresis of the external rectus muscle and a fourth case of rubeosis iridis with melanoma of the choroid and secondary glaucoma.

W. S. Reese.

A Granulation Tumour of the Conjunctiva. J. D. J. Freeman, Brit. J. Ophth. **28:** 277 (June) 1944.

A man aged 30 had the tarsal conjunctiva of the left upper lid covered with multiple pinkish granulomatous nodules, which were glistening and soft in consistency. The retrotarsal fold was not involved. The cornea was not affected. There was no adenopathy. Antituberculosis therapy was instituted, without effect. A tarsectomy was performed. The microscopic examination of the excised tissue showed tissue typical of a granulation tumor of the conjunctiva. There was no evidence of a new growth. No tubercle bacilli were seen. The author discusses the differential diagnosis.

W. Zentmayer.

An Encapsulated Orbital Melanoma. J. Foster, Brit. J. Ophth. **28:** 293 (June) 1944.

The tumor was removed by the transpalpebroconjunctival route of Lagrange, from the right orbit of a woman aged 65. The tumor cells were large, with oval or rounded vesicular nuclei and abundant, slightly granular cytoplasm. Large masses of the cells were sur-

rounded by fibrous septums, continuous with a moderately thick fibrous capsule. There was abundant pigment almost entirely confined to chromatophores in the fibrous septums. Parsons and Loewenstein both expressed the opinion that this tumor was nonmalignant.

W. ZENTMAYER.

Vision

A SIMPLE TEST FOR BINOCULAR FIXATION. S. R. IRVINE, Am. J. Ophth. **27:** 740 (July) 1944.

Irvine gives the following summary of a test for binocular fixation:

"A brief summary of the results of the test is simply that a prism, moved rapidly back and forth before an eye which is contributing to normal binocular vision and fusion, causes diplopia to be noted and produces little or no movement of either eye. The same is true over whichever eye the prism is placed.

"In amblyopia and strabismus, the prism moved in front of the sighting eye induces no diplopia but instead a to-and-fro movement of the image, and conjugate movement of the eyes; whereas a prism before the amblyopic or nonsighting eye may or may not induce diplopia, and results in little or no movement of either eye.

"The above test, requiring no special equipment, provides a quick and decisive method for determining that binocular fixation and fusion are present or that suppression of one eye and dominance of the other exist, findings helpful in the differential diagnosis of amblyopia ex anopsia, minimum strabismus, malingering, or hysteria. In addition it indicates the degree of inhibition existing in amblyopia and strabismus, an estimation which might be of prognostic importance if the good eye were injured." W. S. REESE.

Society Transactions

EDITED BY DR. W. L. BENEDICT

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

FREDERICK C. CORDES, M.D., *Chairman*

BRITTAIN F. PAYNE, M.D., *Secretary*

Fourteenth Scientific Meeting, Chicago, June 13, 1944

Choline Esters with Mydriatic and Cycloplegic Action. DR. KENNETH C. SWAN and MR. NORMAN G. WHITE, Iowa City.

Before a previous meeting of this society, we reported that the corneal penetration of drugs was profoundly affected by their physical properties. For example, the onset and intensity of corneal anesthesia induced by a group of topical anesthetics could be correlated with their surface activity. It was conceived that modifications in physical properties might likewise intensify, or even alter, the ocular effects of autonomic drugs. Choline esters were the first autonomic drugs so modified.

The most characteristic action of previously known choline esters is stimulation of structures innervated by the parasympathetic nervous system; for example, the ocular effects of acetylcholine are miosis and spasm of accommodation resulting from stimulation of the sphincter of the iris and ciliary muscles. Many other choline esters have been synthesized, but in their preparation emphasis was placed on the development of more stable and potent compounds than acetylcholine, such as carbaminoylcholine chloride. The possibility of reversing the characteristic action of acetylcholine did not receive consideration. Moreover, no attempts were made to correlate the pharmacologic action and the physical properties of the choline esters prior to this investigation.

Carbaminoylcholine chloride (doryl), most potent and stable of previously known simple choline esters, was selected for the initial conversion to a surface-active compound. The hydrophilic NH_2 group was replaced by a water-insoluble group, dibutylamine. The resultant surface-active compound, di-n-butylcarbaminoylcholine chloride, was found to have ocular effects the reverse of the action of carbaminoylcholine.

Balance of the hydrophilic quaternary ammonium group in carbaminoylcholine chloride with hydrophobic carbon groups results in a reversal of its pharmacologic action on the intraocular muscles. Whereas carbaminoylcholine chloride produces miosis and cyclotonia, di-n-butylcarbaminoylcholine chloride results in mydriasis and cycloplegia. Correlation of physical properties with the pharmacologic action of other new drugs which we have synthesized indicates that the unique reversal of action of carbaminoylcholine chloride is dependent on its conversion to a surface-active compound. The surface-active carbaminoylcholine derivatives have a potent peripheral antispasmodic action on the smooth muscles of the eye innervated by the parasympathetic nervous system, that is, the sphincter of the iris and the ciliary muscles. The mydriatic and cycloplegic effects of other surface-active choline esters are considerably weaker.

The surface-active carbaminoylcholine derivatives are chemically unrelated to previously known mydriatic and cycloplegic agents—for example, the atropine series—and therefore constitute a new class of drugs. For clinical purposes the sulfate appears to be the most satisfactory salt, and "dibutoline," the most effective member of the new class. It is suggested that the new drugs may act as "inhibitory analogs" of acetylcholine.

Dissociation of Form and Light Perception in Patients with Amblyopia Ex Anopsia. DR. GEORGE WALD and DR. HERMANN M. BURIAN, Boston.

Though it is commonly supposed that amblyopia ex anopsia—loss of vision without perceptible lesion—is due to central suppression of the visual image, the origin and seat of the disability remain uncertain. The absolute threshold of vision was measured under various circumstances in 5 patients with this type of amblyopia. A movable fixation star was provided which could be placed anywhere within a 10 degree radius of the center of the test field. All measurements were monocular and were performed alternately with the normal and the amblyopic eye. The 5 subjects examined were from 10 to 22 years of age. For all of them the corrected vision of the normal eye was 20/25 or better, while that of the amblyopic eye was 20/200 or less.

Three factors were measured: (*a*) dark adaptation in the peripheral fields; (*b*) threshold contours of the completely dark-adapted eye, measured by determination of the threshold for a field 1 degree in diameter, fixated progressively from 10 degrees above to 10 degrees below the fovea, and (*c*) the spectral sensitivity of the dark-adapted retina, measured in peripheral and central fields, including a 1 degree field fixated

centrally so as to fall entirely within the rod-free foveal area.

In all these procedures essentially identical results were obtained with the amblyopic and with the normal eye, both in the fovea and at the periphery. This was true to such a degree that if the experimenter had not known the history of these patients nothing in the course of the measurements would have suggested that their eyes differed in capacity.

None of these patients experienced difficulty in fixating with the amblyopic eye. When the fixation star was presented alternately to the two eyes, none of them remarked any difference in its appearance.

The data themselves prove that fixation by these subjects was truly foveal. Subjects for whom the spectral sensitivity of a 1 degree central field was measured yielded sensitivity functions of the pure cone (photopic) type in both the normal and the amblyopic eye. At the visual threshold this field was seen as colored, further evidence that cones were stimulated. In dark-adapted subjects such an observation can be made only in an exclusively foveal area. The ability of these untrained subjects to confine a 1 degree field wholly within the fovea demonstrated remarkable accuracy of fixation in the amblyopic eye.

It may be concluded that the entire apparatus of light perception is normal in these patients. Their amblyopia appears to be restricted to their perception of pattern.

Quantitative Test for Measurement of the Degree of Red-Green Color Deficiency. DR. LOUISE L. SLOAN, Randolph Field, Texas.

The types of color vision tests needed for the classification of personnel of the Army Air Forces are (1) a simple, rapid and reliable screening test which will distinguish the normal from the color-deficient person and (2) a supplementary quantitative test which will classify the color-deficient subjects as to the degree of the defect and will be of aid in determining whether the applicant is competent to make the color discriminations required in his particular job.

The threshold lantern was devised for use as a supplementary quantitative test. Since recognition of colored light signals is generally considered to be among the most important and the most difficult discriminations required of air crew personnel, a color-naming test was developed which would involve ability to recognize colored lights of low intensity subtending small visual angles.

The instrument uses eight test colors chosen so as to approximate the limiting standards for aviation colors. Each color is shown at eight different levels of intensity, the maximum being approximately one hundred times the minimum. The scores on the test may range from zero to a perfect score of 64. Of 200 normal subjects, 95 per cent made scores of between 60 and 64. The scores for 200 color-deficient subjects ranged from 9 to 64. Twelve per cent of the subjects made scores of 60 or better. The results of second tests were in close agreement with those of the first test and showed no evidence of improvement due to practice.

In order to determine the relation of the scores to ability to recognize light signals under actual conditions, practical field tests were given to both normal and color-deficient subjects. These tests were of two types. The first type involved the identification of red, green and white signals from a traffic control projector; the second, the recognition of colored pyrotechnic signals fired from a plane. When the results of the field tests were compared with scores on several color vision tests giving quantitative scores, it was found that the threshold lantern provided the best indication of success or failure in the field tests.

Backflow Phenomena in Aqueous Veins of Normal and of Glaucomatous Eyes. DR. K. W. ASCHER, Cincinnati.

The entrance of clear fluid into an aqueous vein after experimental blocking of the recipient vessel has been called the positive glass rod phenomenon; in numerous aqueous veins, however, a negative glass rod phenomenon, consisting of entrance of blood into the blocked vessel, has been observed.

The glass rod phenomenon was studied in more than 170 normal eyes (of patients undergoing refraction) and glaucomatous eyes of different types, and the normal eyes were classified according to age of the patient, the results of refraction and the site of the vessel. The refractive condition of the eye and the site of the aqueous vein, but not the age of the patient, appear to be factors bearing on the result of the compression.

The glass rod phenomenon is not an occasional feature and is not produced by transient conditions in the conjunctival or subconjunctival vessels, but is a constant occurrence with an anatomic and physiologic basis; it is the expression of a persistent difference in pressure between two currents of fluid, one being blood and the other aqueous humor mixed with blood at varying ratios.

In eyes with primary compensated glaucoma, the absence of the positive glass rod phenomenon has been confirmed in repeated examinations. Six patients with unilateral compensated primary glaucoma had shallow anterior chambers and normal intraocular pressure in the fellow eye; in all these patients the glass rod phenomenon in the glaucomatous eye was negative, while in the fellow eye, with normal intraocular pressure, aqueous veins, located symmetrically, showed a positive glass rod phenomenon. In eyes with

primary compensated glaucoma, the flow of aqueous humor through the biomicroscopically visible outlets is less vigorous; it may become stronger after successful surgical intervention or after restoration of the intraocular pressure to normal with the use of miotics.

Effect of Chemotherapeutic Agents on Cell Division of the Intact and the Regenerating Corneal Epithelium in the Rat Following Burns and Abrasions. Dr. George K. Smelser and Mr. V. Ozanics, New York.

Healing of standardized corneal burns and abrasions was studied histologically in a large series of rats at frequent stages, ranging from six hours to twelve days. The degrees of injury of the two types were essentially the same. The rate of cell division in the regenerating epithelium received the major emphasis in this study, although the rate at which epithelization was accomplished and the stage at which the normal epithelial thickness was regained were also considered.

After abrasions of the cornea there was rarely an increase in mitosis during the first days after the injury; the defect in the corneal epithelium was filled by cell migration. After thermal burns, however, the rate of cell division notably increased. The elevation of the rate of mitosis persisted for several days. Migration of epithelial cells, however, was an important factor in the healing of thermal burns. These data, which show a difference in the healing processes of two types of corneal injuries, emphasize the importance of avoidance of the local use of substances which inhibit mitosis in the injured cornea. A basis is also established for a study of the effect of drugs in regenerating epithelium with and without elevation of the rate of mitosis.

Extensive corneal abrasions healed without a notable increase in the number of mitotic figures. Thermal burns became covered with epithelium in about the same time as did abrasions (twelve to eighteen hours), but a great increase in the number of mitotic figures was observed during this procedure. Sulfacetimide, sulfapyrazine and penicillin, applied as ointments, powders or solutions, had no effect on cell division in the intact rat cornea. Sulfadiazine tended to increase, and sulfathiazole to depress, cell division in this epithelium. Sulfonamide compounds and penicillin in general had no deleterious effect on cell division in abraded corneas, although the number of mitoses was low in over one-half the sulfathiazole-treated animals. Sulfonamide compounds and penicillin did not interfere with cell division in burned corneal epithelium. Sulfathiazole and sulfacetimide inhibited cell migration after corneal burns, whereas sulfadiazine and penicillin were only slightly detrimental. Sulfonamide ointments inhibited cell migration slightly less than did powders. It is realized that these results are qualified by the form of administration and the relative ability of the compounds to penetrate the cornea.

Use of Penicillin in Military Ophthalmology. Major John G. Bellows, Medical Corps, Army of the United States.

The therapeutic effect of penicillin on experimental ocular infections was studied. Unlike the sulfonamide compounds, penicillin is ineffective when administered orally; therefore there remain but two routes by which the drug can be administered: parenteral, i. e., by intravenous or intramuscular injection, and local, i. e., by subconjunctival or topical application. Since the efficiency of a chemotherapeutic agent depends not only on its potency but on its diffusibility and concentration in the infected tissues, it is of fundamental importance in establishing therapeutic principles to know the distribution and penetration of penicillin into the various ocular tissues and fluids after parenteral or local administration of the drug.

Penicillin reaches the ocular tissues within a few minutes after intravenous injection. After a large dose of penicillin is administered intravenously, it appears in the ocular tissues, in the following decreasing order of concentrations: extraocular muscles, sclera, conjunctiva, blood, tears, chorioretinal layer, aqueous and vitreous humors and cornea. It has never been detected in the crystalline lens. In this respect, the lens is similar to the cerebrospinal fluid, brain and nerve tissues. Local application of penicillin leads to a high concentration of the drug in the tissues of the anterior segment of the globe.

The following ointment bases, in which the penetrability of penicillin was tested, are listed in the order in which they are recommended clinically: a simple ointment, oil in water emulsion and lubricating jelly. The "vanishing" stearate base, in which penicillin seems to have the greatest power of corneal penetration, is not recommended because of its possible damage to the corneal epithelium. However, it may be used on the skin of the lids.

Penicillin was effective in the clinical treatment of acute and chronic infections of the lids, conjunctiva and cornea produced by penicillin-sensitive organisms. It was ineffective in 2 cases of exudative choroiditis of undetermined origin and in 1 case of gonorrheal iridocyclitis. Susceptible persons may become hypersensitive to penicillin.

Corneal Healing: The Adhesive Power of Aqueous Fibrin in the Rabbit; Preliminary Report. Dr. Albert L. Brown and Dr. Frank A. Nantz, Cincinnati.

While studying the placement of sutures in incisions in the rabbit cornea, we were attracted by the firm apposition of the edges of the wound before actual healing began. The sutures were not in any degree responsible for this firm ap-

proximation, as attested by the effects of their removal and then of their omission. An incision in the cornea proper engages no blood vessels. There is no adjacent structure or substance adjacent to such an incision except the aqueous. It therefore remained for us to determine the quantitative and qualitative adhesive power of the aqueous for corneal wounds.

The edges of the wound after an incision in the rabbit cornea are approximated strongly by the secondary aqueous. A wound surrounding a transplant will support eleven thousand times the weight of the transplant in four hours. This sealing is accomplished by the fibrin produced in the aqueous. The aqueous fibrin is a product of the union of thrombin from the edges of the wound and fibrinogen in the aqueous. Heparin was injected into the anterior chamber to replace aspirated aqueous. This agent strikingly decreased the adhesive power of the secondary aqueous after corneal incision. The heparin was then replaced by thrombin and fibrinogen, and the adhesive power was restored. No comparable action occurs in man. Human aqueous shows no more than a trace of fibrinogen and a correspondingly diminished adhesive power.

News and Notes

GENERAL NEWS

Ophthalmologic Seminar, Emory University School of Medicine.—On April 19-21, 1945 Emory University, Atlanta, Ga., will celebrate the one-hundredth anniversary of the birth of Abner Wellborn Calhoun, M.D., LL.D., born April 16, 1845, died Aug. 21, 1910, the first professor of ophthalmology of the Atlanta Medical College, which was established in 1845 and in 1915 became the Emory University School of Medicine.

Dr. Calhoun was a pioneer in southern ophthalmology and was generous of his time and means for the advancement of medical education and ophthalmology.

All guests are invited to the luncheons and dinners, so that they may become better acquainted with the speakers. The dress at all functions will be informal, and there will be no fees. Reservations should be made early at the Biltmore Hotel. Those physicians who plan to attend are requested to notify the Dean, Dr. Russell Oppenheimer (50 Armstrong Street, Atlanta, Ga.), at what meals they will be present, so that necessary arrangements can be made.

At the ophthalmologic seminar honoring his memory, the guest lecturers will be: Dr. William L. Benedict, Dr. John H. Dunnington, Dr. Harry S. Gradle, Dr. Parker Heath, Dr. Walter I. Lillie, Colonel Derrick Vail and Dr. Frank B. Walsh.

Pan-American Congress of Ophthalmology.—Dr. Harry S. Gradle, president of the Second Pan-American Congress of Ophthalmology, who is now in South America on a speaking tour, has found all the leading ophthalmologists in Latin America enthusiastic about the next meeting of the congress, which is scheduled for Nov. 25 to 30, 1945, in Montevideo, Uruguay. He has met with various Latin-American officers of the congress and with the committee on arrangements in Montevideo, and reports that the program is set up and that all preliminary arrangements have been completed.

Book Reviews

The Practice of Orthoptics. By G. H. Giles, F.B.O.A. (Hon.), F.S.M.C. Price, 25 shillings. Pp. 366, with 67 illustrations. London: Hammond, Hammond, Hammond & Company, Ltd., 1943.

This volume is an amplification of the author's "Manual of Practical Orthoptics," published in 1938. The inclusion of a chapter on the "Orthoptic Treatment of Service Candidates," with special emphasis on the ocular requirements for aviation candidates, provides a timely addition.

Mr. Giles, a member of the staff of the London Refraction Hospital, is an optical practitioner (optometrist in America), and references throughout the text indicate that he has written it primarily for use by optical practitioners. His point of view may be illustrated by the following quotation: "The method developed by Worth is still the basis of most of the work of present day medical orthoptists, but advanced workers, particularly those outside the medical profession, do not now completely accept his teaching."

Mr. Giles is an ardent disciple of Cantonnet. The Remy separator and the Pigeon-Cantonnet stereoscope are his basic training instruments. Such a fundamental instrument as a major amblyoscope, designated by him as a "synotype instrument," plays only a secondary role in his technic and is not listed in the equipment essential for orthoptic training.

The author errs on the side of conservatism in the selection of patients whom he considers suitable for orthoptic treatment. Although Cantonnet set the upper limit of the degree of concomitant squint as 35 to 40 degrees, he does not consider one of more than 25 degrees amenable to orthoptic training. According to him, other factors militating against a successful outcome of such treatments are appearance of squint before the age of 2 years and sudden onset of the condition.

Because of the emphasis placed on "mental effort," the Cantonnet technic is not suitable for treating children under 7 years of age. Mr. Giles prefers to postpone systematic treatments until this age is reached whenever possible. When this is not possible, he is forced to accept the methods of the so-called medical orthoptists, conceding that "with children under seven, it is often necessary to treat the strabismus by the older methods of Worth and modified more recently by Lyle and Jackson."

The upper age limit for treatment of squints is given as 20 to 30 years, and that for the treatment of heterophorias, as 40 to 45. It is surprising to find the prescription of prisms advocated for heterophorias in patients beyond the age of 45, for in the United States it is generally accepted that convergence insufficiency associated with the wearing of a first correction for presbyopia responds more readily to orthoptic treatment than any other type of ocular imbalance.

To one who relies on a major amblyoscope as a basic training instrument, this practitioner's delay in testing retinal correspondence until the second stage of treatment has been completed, i. e., until simultaneous vision for form has been restored, seems fraught with the potential danger that an undiagnosed abnormal retinal correspondence will be reenforced. In regard to this possibility, Mr. Giles maintains that "the abnormal retinal correspondence appears to coincide with the existence of a suppression area or scotoma which is manifested when a first attempt is made to use both eyes together. With the disappearance of this suppression area, simultaneous vision is restored, and in most cases there exists no abnormal retinal correspondence."

A major amblyoscope is admittedly the most satisfactory instrument for diagnosis and treatment of abnormal retinal correspondence, but methods for adapting the Pigeon-Cantonnet stereoscope for both these purposes are described, the results in diagnosis being "only slightly less accurate than with the synotype instruments."

This book should serve as a satisfactory elucidation of Cantonnet's technic to any one interested in applying this method of orthoptic training. On the other hand, it cannot be recommended as a text for candidates who wish to qualify for certification by the American Orthoptic Council.

ELIZABETH K. STARK.

Technique of Fitting Contact Lenses. By Albert L. Anderson. Pp. 71, with 33 illustrations. Minneapolis: McGill Lithograph Co., 1944.

This booklet describes the technic of fitting plastic contact lenses by means of impressions taken from the living eye. The author recommends the use of tetracaine and epinephrine to provide anesthesia and to reduce congestion. The cast is then taken with a molding powder and a plastic lens prepared from the mold. No description of the manufacture of the lens is given, the remainder of the book being devoted to methods of adjusting the lens, instructions to the patient and the composition of the solutions employed.

This treatise is essentially practical in content, little attention being given to theory. The exposition is clear, and the illustrations, mostly photographic, are excellent. The book is of value only as a guide because such involved technical procedures are learned only under the supervision of an experienced teacher.

G. M. BRUCE.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Dr. P. Bailliart, 66 Boulevard Saint-Michel, Paris, 6e, France.
Secretary-General: Prof. M. Van Duyse, Université de Gand, Gand, Prov. Ostflandern, Belgium.
All correspondence should be addressed to the Secretariat, 66 Boulevard Saint-Michel, Paris, 6e, France.

International Ophthalmologic Congress

President: Prof. Nordenson, Serafimerlasarettet, Stockholm, Sweden.
Secretary: Dr. Ehlers, Jerbanenegade 41, Copenhagen, Denmark.

International Organization Against Trachoma

President: Dr. A. F. MacCallan, 17 Horseferry Rd., London, England.

Pan-American Congress of Ophthalmology

President: Dr. Harry S. Gradle, 58 E. Washington St., Chicago.
Executive Secretaries: Dr. Conrad Berens, 35 E. 70th St., New York. Dr. M. E. Alvaro, 1511 Rua Consolacão, São Paulo, Brazil.

FOREIGN

All-India Ophthalmological Society

President: Dr. B. K. Narayan Rao, Minto Ophthalmic Hospital, Bangalore.
Secretary: Dr. G. Zachariah, Flitcham, Marshall's Rd., Madras.

British Medical Association, Section on Ophthalmology

President: Dr. W. Clark Souter, 9 Albyn Pl., Aberdeen, Scotland.
Secretary: Dr. Frederick Ridley, 12 Wimpole St., London, W. 1.

Chengtu Ophthalmological Society

President: Dr. Eugene Chan.
Secretary: Dr. K. S. Sun.
Place: Eye, Ear, Nose and Throat Hospital, Chengtu, China.

Chinese Ophthalmology Society

President: Dr. C. H. Chou, 363 Avenue Haig, Shanghai.
Secretary: Dr. F. S. Tsang, 221 Foochow Rd., Shanghai.

Chinese Ophthalmological Society of Peiping

President: Dr. H. T. Pi, Peiping Union Medical College, Peiping.
Secretary: Dr. C. K. Lin, 180 Hsi-Lo-yen Chienmeng, Peiping.
Place: Peiping Union Medical College, Peiping. Time: Last Friday of each month.

German Ophthalmological Society

President: Prof. W. Lohlein, Berlin.
Secretary: Prof. E. Engelking, Heidelberg.

Hungarian Ophthalmological Society

President: Prof. I. Imre, Budapest.
Assistant Secretary: Dr. Stephen de Grósz, University Eye Hospital, Máriautca 39, Budapest.
All correspondence should be addressed to the Assistant Secretary.

Midland Ophthalmological Society

President: Dr. W. Niccol, 4 College Green, Gloucester, England.
Secretary: Mr. T. Harrison Butler, 61 Newhall St., Birmingham 3, England.
Place: Birmingham and Midland Eye Hospital.

North of England Ophthalmological Society

President: Mr. John Foster, 45 Park Sq., Leeds.
Secretary: Mr. William M. Muirhead, 70 Upper Hanover St., Sheffield.
Place: Manchester, Bradford, Leeds, Newcastle-upon-Tyne, Liverpool and Sheffield, in rotation. Time: October to April.

Ophthalmological Society of Australia

President: Dr. A. James Flynn, 135 Macquarie St., Sydney.
Secretary: Dr. D. Williams, 193 Macquarie St., Sydney.

Ophthalmological Society of Egypt

President: Prof. Dr. Mohammed Mahfouz Bey, Government Hospital, Alexandria.
Secretary: Dr. Mohammed Khalil, 4 Baehler St., Cairo.
All correspondence should be addressed to the secretary, Dr. Mohammed Khalil.

Ophthalmological Society of the United Kingdom

President: Mr. Charles B. Goulden, 89 Harley St., London.
Secretary: Mr. Frank W. Law, 30 Devonshire Pl., London, W. 1.

Ophthalmology Society of Bombay

President: Dr. D. D. Sathaye, 127 Girgaum Rd., Bombay 4, India.
Secretary: Dr. H. D. Dastur, Dadar, Bombay 14, India.
Place: H. B. A. Free Ophthalmic Hospital, Parel, Bombay 12. Time: First Friday of every month.

Oxford Ophthalmological Congress

Master: Mr. P. G. Doyne, 60 Queen Anne St., London, W. 1, England.
Secretary-Treasurer: Dr. F. A. Anderson, 12 St. John's Hill, Shrewsbury, England.

Palestine Ophthalmological Society

President: Dr. Arieh Feigenbaum, Abyssinian St. 15, Jerusalem.
Secretary: Dr. E. Sinai, Tel Aviv.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and keep it up to date.

POLISH OPHTHALMOLOGICAL SOCIETY

President: Dr. W. Kapuściński, 2 Waly Batorego, Poznań.
Secretary: Dr. J. Sobański, Lindley'a 4, Warsaw.
Place: Lindley'a 4, Warsaw.

ROYAL SOCIETY OF MEDICINE, SECTION OF OPHTHALMOLOGY

President: Col. F. A. Juler, 96 Harley St., London, W. 1, England.
Secretary: Dr. Harold Ridley, 60 Queen Anne St., London, W. 1, England.

SÃO PAULO SOCIETY OF OPHTHALMOLOGY

President: Prof. Moacyr E. Alvaro, Consolação 1151, São Paulo, Brazil.
Secretary: Dr. Silvio de Almeida Toledo, Enfermaria Santo Luzia, Santa Casa de Misericordia, Cesario Motta, St. 112, São Paulo, Brazil.

SCOTTISH OPHTHALMOLOGICAL CLUB

President: Dr. S. Spence Meighan, 13 Woodside Pl., Glasgow, C. 3.
Secretary: Dr. Alexander Garrow, 15 Woodside Pl., Glasgow, C. 3.
Place: Edinburgh and Glasgow, in rotation.

SOCIEDAD ARGENTINA DE OFTALMOLOGIA

Chairman: Dr. Jorge Malbrán, Buenos Aires.
Secretary: Dr. Benito Just Tiscornia, Santa Fe 1171, Buenos Aires.

SOCIEDAD OFTALMOLOGIA DEL LITORAL, ROSARIO (ARGENTINA)

President: Prof. Dr. Carlos Weskamp, Laprida 1159, Rosario.
Secretary: Dr. Juan M. Vila Ortiz, Córdoba 1433, Rosario.
Place: Rosario. Time: Last Saturday of every month, April to November, inclusive. All correspondence should be addressed to the President.

SOCIEDADE DE OFTALMOLOGIA DE MINAS GERAIS

President: Prof. Hilton Rocha, Rua Rio de Janeiro 2251, Bello Horizonte, Minas Geraes, Brazil.
Secretary: Dr. Ennio Coscarelli, Rua Aimorés 1697, Bello Horizonte, Minas Geraes, Brazil.

SOCIEDADE DE OFTALMOLOGIA E OTORRINOLARINGOLOGIA DE RIO GRANDE DO SUL

President: Dr. Luiz Assumpção Osorio, Edificio Vera Cruz, Apartamento 134, Porto Alegre, Rio Grande do Sul.
Secretary: Dr. Fernando Voges Alves, Caixa Postal 928, Porto Alegre, Rio Grande do Sul.

SOCIEDADE DE OPHTHALMOLOGIA E OTO-RHINO-LARYNGOLOGIA DA BAHIA

President: Dr. Theonilo Amorim, Barra Avenida, Bahia, Brazil.
Secretary: Dr. Adroaldo de Alencar, Brazil.
All correspondence should be addressed to the President.

SOCIETÀ OFTALMOLOGICA ITALIANA

President: Prof. Dott. Giuseppe Ovio, Ophthalmological Clinic, University of Rome, Rome.
Secretary: Prof. Dott. Epimaco Leonardi, Via del Gianicolo, 1, Rome.

SOCIÉTÉ FRANÇAISE D'OPHTALMOLOGIE

Secretary: Dr. René Onfray, 6 Avenue de la Motte Picquet, Paris, 7e.

SOCIETY OF SWEDISH OPHTHALMOLOGISTS

President: Prof. K. G. Ploman, Stockholm.
Secretary: Dr. K. O. Granström, Södermalmstorg 4 Ill tr., Stockholm, Sö.

TEL AVIV OPHTHALMOLOGICAL SOCIETY

President: Dr. D. Arieh-Friedman, 96 Allenby St., Tel Aviv, Palestine.
Secretary: Dr. Sadger Max, 9 Bialik St., Tel Aviv, Palestine.

NATIONAL

AMERICAN MEDICAL ASSOCIATION, SCIENTIFIC ASSEMBLY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Frederick C. Cordes, 384 Post St., San Francisco.
Secretary: Dr. R. J. Masters, 23 E. Ohio St., Indianapolis.
In compliance with the request of the Office of Defense Transportation and in the interest of the national war effort a meeting will not be held in 1945.

AMERICAN ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY, SECTION ON OPHTHALMOLOGY

President: Dr. Gordon B. New, Mayo Clinic, Rochester, Minn.
President-Elect: Dr. Alan C. Woods, Johns Hopkins Hospital, Baltimore 5.
Executive Secretary-Treasurer: Dr. William L. Benedict, 100–1st Ave. Bldg., Rochester, Minn.

AMERICAN OPHTHALMOLOGICAL SOCIETY

President: Dr. S. Judd Beach, 704 Congress St., Portland, Maine.
Secretary-Treasurer: Dr. Walter S. Atkinson, 129 Clinton St., Watertown, N. Y.

ASSOCIATION FOR RESEARCH IN OPHTHALMOLOGY, INC.

Chairman: Dr. Conrad Berens, 35 E. 70th St., New York.
Secretary-Treasurer: Major Brittain F. Payne, School of Aviation Medicine, Randolph Field, Texas.
Assistant Secretary-Treasurer: Dr. Hunter Romaine, 35 E. 70th St., New York.

CANADIAN MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY

President: Dr. Alexander E. MacDonald, 170 St. George St., Toronto.
Secretary-Treasurer: Dr. L. J. Sebert, 170 St. George St., Toronto.

CANADIAN OPHTHALMOLOGICAL SOCIETY

President: Dr. R. Evatt Mathers, 34½ Morris St., Halifax, N. S.
Secretary-Treasurer: Dr. Kenneth B. Johnston, Suite 1, 1509 Sherbrooke St. W., Montreal.

NATIONAL SOCIETY FOR THE PREVENTION OF BLINDNESS

President: Mr. Mason H. Bigelow, 1790 Broadway, New York.
Secretary: Miss Regina E. Schneider, 1790 Broadway, New York.
Executive Director: Mrs. Eleanor Brown Merrill, 1790 Broadway, New York.

SECTIONAL

ACADEMY OF MEDICINE OF NORTHERN NEW JERSEY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. N. Zwaifler, 46 Wilbur Ave., Newark.
Secretary: Dr. William F. Keim Jr., 25 Roseville Ave., Newark.
Place: 91 Lincoln Park South, Newark. Time: 8:45 p. m., second Monday of each month, October to May.

CENTRAL ILLINOIS SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. Watson Gailey, 1000 N. Main St., Bloomington, Ill.
Secretary-Treasurer: Dr. William F. Hubble, 861-867 Citizens Bldg., Decatur, Ill.

CENTRAL WISCONSIN SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. J. Friend, 425 E. Grand Ave., Beloit, Wis.
Secretary: Dr. G. L. McCormick, 626 S. Central Ave., Marshfield.

NEW ENGLAND OPHTHALMOLOGICAL SOCIETY

President: Dr. Paul A. Chandler, 5 Bay State Rd., Boston.
Secretary-Treasurer: Dr. Merrill J. King, 264 Beacon St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

PACIFIC COAST OTO-OPHTHALMOLOGICAL SOCIETY

President: Dr. D. H. O'Rourke, 1612 Tremont Pl., Denver.
Secretary-Treasurer: Dr. C. Allen Dickey, 450 Sutter St., San Francisco.

PUGET SOUND ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. James H. Mathews, 1317 Marion St., Seattle, Wash.
Secretary-Treasurer: Dr. Barton E. Peden, 301 Stimson Bldg., Seattle 1.
Place: Seattle or Tacoma, Wash. Time: Third Tuesday of each month except June, July and August.

ROCK RIVER VALLEY EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. J. Sheldon Clark, 27 E. Stephenson St., Freeport, Ill.
Secretary-Treasurer: Dr. Harry R. Warner, 321 W. State St., Rockford, Ill.
Place: Rockford, Ill., or Janesville or Beloit, Wis. Time: Third Tuesday of each month from October to April, inclusive.

SAGINAW VALLEY ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. L. D. Gomon, 308 Eddy Bldg., Saginaw, Mich.
Secretary-Treasurer: Dr. Harold H. Heuser, 207 Davidson Bldg., Bay City, Mich.
Place: Saginaw or Bay City, Mich. Time: Second Tuesday of each month, except July, August and September.

SIOUX VALLEY EYE AND EAR ACADEMY

President: Dr. J. C. Decker, 515 Francis Bldg., Sioux City, Iowa.
Secretary-Treasurer: Dr. J. E. Dvorak, 408 Davidson Bldg., Sioux City, Iowa.

SOUTHERN MEDICAL ASSOCIATION, SECTION ON EYE, EAR, NOSE AND THROAT

Chairman: Dr. John H. Burleson, 414 Navarro St., San Antonio, Texas.
Secretary: Dr. J. W. Jervey Jr., 101 Church St., Greenville, S. C.

SOUTHWESTERN ACADEMY OF EYE, EAR, NOSE AND THROAT

President: Dr. H. L. Brehmer, 221 W. Central Ave., Albuquerque, N. Mex.
Secretary: Dr. A. E. Cruthirds, 1011 Professional Bldg., Phoenix, Ariz.

SOUTHWESTERN MICHIGAN TRIOLOGICAL SOCIETY

President: Dr. W. M. Dodge, 716 First National Bank Bldg., Battle Creek.
Secretary-Treasurer: Dr. Kenneth Lowe, 25 W. Michigan Ave., Battle Creek.
Time: Last Thursday of September, October, November, March, April and May.

WESTERN PENNSYLVANIA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. Ray Parker, 218 Franklin St., Johnston, Pa.
Secretary-Treasurer: Dr. J. McClure Tyson, Deposit Nat'l Bank Bldg., DuBois.

STATE

ARKANSAS STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. Raymond C. Cook, 701 Main St., Little Rock.
Secretary: Dr. K. W. Cosgrove, Urquhart Bldg., Little Rock.

COLORADO OPHTHALMOLOGICAL SOCIETY

President: Dr. C. A. Ringle, 912-9th Ave., Greeley.
Secretary: Dr. W. A. Ohmart, 1102 Republic Bldg., Denver.
Place: University Club, Denver. Time: 7:30 p. m., third Saturday of each month, October to May, inclusive.

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON EYE, EAR, NOSE AND THROAT

President: Dr. F. L. Phillips, 405 Temple St., New Haven.
Secretary-Treasurer: Dr. W. H. Turnley, 1 Atlantic St., Stamford, Conn.

EYE, EAR, NOSE AND THROAT CLUB OF GEORGIA

President: William O. Martin Jr., Doctors Bldg., Atlanta.
Secretary-Treasurer: Dr. C. K. McLaughlin, 526 Walton St., Macon.

INDIANA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. F. McK. Ruby, Union City.
Secretary: Dr. Edwin W. Dyar Jr., 23 E. Ohio St., Indianapolis.
Place: French Lick. Time: First Wednesday in April.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. J. K. Von Lackum, 117–3d St. S. E., Cedar Rapids.
Secretary-Treasurer: Dr. B. M. Merkel, 604 Locust St., Des Moines.

Kansas State Medical Society, Section on Ophthalmology and Otolaryngology

President: Dr. W. D. Pittman, Pratt.
Secretary: Dr. Louis R. Haas, 902 N. Broadway, Pittsburg.

Louisiana-Mississippi Ophthalmological and Otolaryngological Society

President: Dr. Val. H. Fuchs, 200 Carondelet St., New Orleans.
Secretary-Treasurer: Dr. Edley H. Jones, 1301 Washington St., Vicksburg, Miss.

Michigan State Medical Society, Section of Ophthalmology and Otolaryngology

Chairman: Dr. Robert H. Fraser, 25 W. Michigan Ave., Battle Creek.
Secretary: Dr. R. G. Laird, 114 Fulton St., Grand Rapids.

Minnesota Academy of Ophthalmology and Otolaryngology

President: Dr. George E. McGeary, 920 Medical Arts Bldg., Minneapolis.
Secretary: Dr. William A. Kennedy, 372 St. Peter St., St. Paul.
Time: Second Friday of each month from October to May.

Montana Academy of Oto-Ophthalmology

President: Dr. William Morrison, 208 N. Broadway, Billings.
Secretary: Dr. Fritz D. Hurd, 309 Medical Arts Bldg., Great Falls.

Nebraska Academy of Ophthalmology and Otolaryngology

President: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Secretary-Treasurer: Dr. John Peterson, 1307 N. St., Lincoln.

New Jersey State Medical Society, Section on Ophthalmology, Otology and Rhinolaryngology

Chairman: Dr. George P. Meyer, 410 Haddon Ave., Camden.
Secretary: Dr. John P. Brennan, 429 Cooper St., Camden.

New York State Medical Society, Eye, Ear, Nose and Throat Section

Chairman: Dr. Harold J. Joy, 504 State Tower Bldg., Syracuse 2.
Secretary: Dr. Maxwell D. Ryan, 660 Madison Ave., New York 21.

North Carolina Eye, Ear, Nose and Throat Society

President: Dr. Hugh C. Wolfe, 102 N. Elm St., Greensboro.
Secretary: Dr. Vanderbilt F. Couch, 104 W. 4th St., Winston-Salem.

North Dakota Academy of Ophthalmology and Oto-Laryngology

President: Dr. W. L. Diven, City National Bank Bldg., Bismarck.
Secretary-Treasurer: Dr. A. E. Spear, 20 W. Villard, Dickenson.

Oregon Academy of Ophthalmology and Oto-Laryngology

President: Dr. Paul Neely, 1020 S. W. Taylor St., Portland.
Secretary-Treasurer: Dr. Lewis Jordon, 1020 S. W. Taylor St., Portland.
Place: Good Samaritan Hospital, Portland. Time: Third Tuesday of each month.

Pennsylvania Academy of Ophthalmology and Otolaryngology

President: Dr. Lewis T. Buckman, 83 S. Franklin St., Wilkes-Barre.
Secretary Pro Tem: Dr. Paul C. Craig, 232 N. 5th St., Reading.
Time: Last week in April.

Rhode Island Ophthalmological and Otological Society

Acting President: Dr. N. Darrell Harvey, 112 Waterman St., Providence.
Secretary-Treasurer: Dr. Linley C. Happ, 124 Waterman St., Providence.
Place: Rhode Island Medical Society, Library, Providence. Time: 8:30 p. m., second Thursday in October, December, February and April.

South Carolina Society of Ophthalmology and Otolaryngology

President: Dr. J. L. Sanders, 222 N. Main St., Greenville.
Secretary: Dr. J. H. Stokes, 125 W. Cheves St., Florence.

Tennessee Academy of Ophthalmology and Otolaryngology

President: Dr. Wesley Wilkerson, 700 Church St., Nashville.
Secretary-Treasurer: Dr. W. D. Stinson, 124 Physicians and Surgeons Bldg., Memphis.

Texas Ophthalmological and Oto-Laryngological Society

President: Dr. F. H. Rosebrough, 603 Navarro St., San Antonio.
Secretary: Dr. M. K. McCullough, 1717 Pacific Ave., Dallas.

Utah Ophthalmological Society

President: Dr. R. B. Maw, 699 E. South Temple, Salt Lake City.
Secretary-Treasurer: Dr. Charles Ruggeri Jr., 1120 Boston Bldg., Salt Lake City.
Place: University Club, Salt Lake City. Time: 7:00 p. m., third Monday of each month.

Virginia Society of Oto-Laryngology and Ophthalmology

President: Dr. Mortimer H. Williams, 30½ Franklin Rd. S. W., Roanoke.
Secretary-Treasurer: Dr. Meade Edmunds, 34 Franklin St., Petersburg.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. George Traugh, 309 Cleveland Ave., Fairmont.

Secretary: Dr. Welch England, 621½ Market St., Parkersburg.

LOCAL

AKRON ACADEMY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. E. L. Mather, 39 S. Main St., Akron, Ohio.

Secretary-Treasurer: Dr. V. C. Malloy, 2d National Bank Bldg., Akron, Ohio.

Time: First Monday in January, March, May and November.

ATLANTA EYE, EAR, NOSE AND THROAT SOCIETY

President: Dr. B. M. Cline, 153 Peachtree St. N. E., Atlanta, Ga.

Acting Secretary: Dr. A. V. Hallum, 478 Peachtree St. N. E., Atlanta, Ga.

Place: Grady Hospital. Time: 6:00 p. m., fourth Monday of each month, from October to May.

BALTIMORE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY

Chairman: Dr. Ernst Bodenheimer, 1212 Eutaw Pl., Baltimore.

Secretary: Dr. Thomas R. O'Rourk, 104 W. Madison St., Baltimore.

Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to March.

BIRMINGHAM EYE, EAR, NOSE AND THROAT CLUB

President: Each member, in alphabetical order.

Secretary: Dr. Luther E. Wilson, 919 Woodward Bldg., Birmingham, Ala.

Place: Tutwiler Hotel. Time: 6:30 p. m., second Tuesday of each month, September to May, inclusive.

BROOKLYN OPHTHALMOLOGICAL SOCIETY

President: Dr. Michael J. Buonaguro, 589 Lorimer St., Brooklyn.

Secretary-Treasurer: Dr. Benjamin C. Rosenthal, 140 New York Ave., Brooklyn 16.

Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

BUFFALO OPHTHALMOLOGIC CLUB

President: Dr. Walter F. King, 519 Delaware Ave., Buffalo.

Secretary-Treasurer: Dr. Sheldon B. Freeman, 196 Linwood Ave., Buffalo.

Time: Second Thursday of each month.

CHATTANOOGA SOCIETY OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Each member, in alphabetical order.

Secretary: Dr. Douglas Chamberlain, Chattanooga Bank Bldg., Chattanooga, Tenn.

Place: Mountain City Club. Time: Second Thursday of each month from September to May.

CHICAGO OPHTHALMOLOGICAL SOCIETY

President: Dr. Samuel J. Meyer, 58 E. Washington St., Chicago 2.

Secretary: Dr. W. A. Mann, 30 N. Michigan Ave., Chicago 2.

Place: Continental Hotel, 505 N. Michigan Ave. Time: Third Monday of each month from October to May.

CINCINNATI GENERAL HOSPITAL OPHTHALMOLOGY STAFF

Chairman: Dr. D. T. Vail, 441 Vine St., Cincinnati.

Secretary: Dr. A. A. Levin, 441 Vine St., Cincinnati.

Place: Cincinnati General Hospital. Time: 7:45 p. m., third Friday of each month except June, July and August.

CLEVELAND OPHTHALMOLOGICAL CLUB

Chairman: Dr. Shandor Monson, 1621 Euclid Ave., Cleveland.

Secretary: Dr. Carl Ellenberger, 14805 Detroit Ave., Cleveland.

Time: Second Tuesday in October, December, February and April.

COLLEGE OF PHYSICIANS, PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Chairman: Dr. W. S. Reese, 1901 Walnut St., Philadelphia.

Clerk: Dr. George F. J. Kelly, 37 S. 20th St., Philadelphia.

Time: Third Thursday of every month from October to April, inclusive.

COLUMBUS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

Chairman: Dr. Erwin W. Troutman, 21 E. State St., Columbus, Ohio.

Secretary-Treasurer: Dr. T. Rees Williams, 380 E. Town St., Columbus 15, Ohio.

Place: University Club. Time: 6:15 p. m., first Monday of each month, from October to May, inclusive.

CORPUS CHRISTI EYE, EAR, NOSE AND THROAT SOCIETY

Chairman: Dr. C. B. Collins, 704 Medical Professional Bldg., Corpus Christi, Texas.

Secretary: Dr. L. W. O. Janssen, 710 Medical Professional Bldg., Corpus Christi, Texas.

Time: 6:30 p. m., third Tuesday of each month from October to May.

DALLAS ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Ruby K. Daniel, Medical Arts Bldg., Dallas 1, Texas.

Secretary: Dr. Tom Barr, Medical Arts Bldg., Dallas 1, Texas.

Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. H. C. Schmitz, 604 Locust St., Des Moines, Iowa.

Secretary-Treasurer: Dr. Byron M. Merkel, 604 Locust St., Des Moines, Iowa.

Time: 7:45 p. m., third Monday of every month from September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.

Secretary: Dr. Cecil W. Lepard, 1025 David Whitney Bldg., Detroit 26.

Place: Club rooms of Wayne County Medical Society.

Time: First Wednesday of each month, November to April, inclusive.

Detroit Ophthalmological Society

President: Dr. Raymond S. Goux, 545 David Whitney Bldg., Detroit 26.

Secretary: Dr. Arthur Hale, 1609 Eaton Tower, Detroit 26.

Place: Club rooms of Wayne County Medical Society. Time: 6:30 p. m., third Thursday of each month from November to April, inclusive.

Eastern New York Eye, Ear, Nose and Throat Association

President: Appointed at each meeting.

Secretary-Treasurer: Dr. Joseph L. Holohan, 330 State St., Albany.

Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. Rex Howard, 602 W. 10th St., Fort Worth, Texas.

Secretary-Treasurer: Dr. R. H. Gough, Medical Arts Bldg., Fort Worth, Texas.

Place: Medical Hall, Medical Arts Bldg. Time: 7:30 p. m., first Friday of each month except July and August.

Houston Academy of Medicine, Ophthalmological and Oto-Laryngological Section

President: Dr. Lyle J. Logue, 1304 Walker Ave., Houston, Texas.

Secretary: Dr. John T. Stough, 803 Medical Arts Bldg., Houston, Texas.

Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., second Thursday of each month from September to June.

Indianapolis Ophthalmological and Oto-laryngological Society

President: Dr. Myron Harding, 23 E. Ohio St., Indianapolis.

Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.

Place: Indianapolis Athletic Club. Time: 6:30 p. m., second Thursday of each month from November to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Edgar Johnson, 906 Grand Ave., Kansas City, Mo.

Secretary: Dr. W. E. Keith, 1103 Grand Ave., Kansas City, Mo.

Time: Third Thursday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

Chairman: Dr. Harold Snow, 614 S. Pacific Ave., San Pedro, Calif.

Secretary-Treasurer: Dr. Oliver R. Nees, 508 Times Bldg., Long Beach, Calif.

Place: Professional Bldg. Time: Last Wednesday of each month from October to May.

Los Angeles Society of Ophthalmology and Otolaryngology

President: Dr. Orrie E. Ghrist, 210 N. Central Ave., Glendale, Calif.

Secretary-Treasurer. Dr. K. C. Brandenburg, 110 Pine Ave., Long Beach 2, Calif.

Place: Los Angeles County Medical Association Bldg., 1925 Wilshire Blvd. Time: 6:00 p. m., fourth Monday of each month from September to May, inclusive.

Louisville Eye and Ear Society

President: Dr. Joseph S. Heitger, Heyburn Bldg., Louisville, Ky.

Secretary-Treasurer: Dr. J. W. Fish, 321 W. Broadway, Louisville, Ky.

Place: Brown Hotel. Time: 6:30 p. m., second Thursday of each month from September to May, inclusive.

Lower Anthracite Eye, Ear, Nose and Throat Society

Chairman: Each member in alphabetical order.

Secretary: Dr. James J. Monohan, 31 S. Jardin St., Shenandoah, Pa.

Medical Society of the District of Columbia, Section of Ophthalmology and Otolaryngology

Chairman: Dr. P. S. Constantinople, 1835 I St. N. W., Washington.

Secretary: Dr. Frazier Williams, 1801 I St. N. W., Washington.

Place: 1718 M St. N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Otolaryngology

Chairman: Each member in alphabetical order.

Secretary: Dr. Sam H. Sanders, 1089 Madison Ave., Memphis, Tenn.

Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month from September to May.

Milwaukee Oto-Ophthalmic Society

President: Dr. Leon H. Guerin, 324 E. Wisconsin Ave., Milwaukee 2.

Secretary-Treasurer: Dr. Frank G. Treskow, 411 E. Mason St., Milwaukee 2.

Place: University Club. Time: 6:30 p. m., fourth Tuesday of each month from October to May.

Montgomery County Medical Society

Chairman: Dr. H. V. Dutrow, 1040 Fidelity Medical Bldg., Dayton, Ohio.
Secretary-Treasurer: Dr. Maitland D. Place, 981 Reibold Bldg., Dayton, Ohio.
Place: Van Cleve Hotel. Time: 6:30 p. m., first Tuesday of each month from October to June, inclusive.

Montreal Ophthalmological Society

President: Dr. J. Rosenbaum, 1396 Ste. Catherine St. W., Montreal, Canada.
Secretary: Dr. L. Tessier, 1230 St. Joseph Blvd. E., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. M. M. Cullom, 700 Church St., Nashville, Tenn.
Secretary: Dr. R. E. Sullivan, 432 Doctors Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month from October to May.

New Haven Ophthalmological Society

President: Dr. William H. Ryder, 185 Church St., New Haven, Conn.
Secretary: Dr. Frederick A. Wiess, 255 Bradley St., New Haven, Conn.

New Orleans Ophthalmological and Oto-Laryngological Society

President: Dr. W. B. Clark, 1012 American Bank Bldg., New Orleans.
Secretary: Dr. Mercer G. Lynch, 1018 Maison Blanche Bldg., New Orleans.
Place: Louisiana State University Medical Bldg. Time: 8 p. m., second Tuesday of each month from October to May.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Thomas H. Johnson, 30 W. 59th St., New York.
Secretary: Dr. Wendell L. Hughes, 131 Fulton Ave., Hempstead, N. Y.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

New York Society for Clinical Ophthalmology

President: Dr. Milton Berliner, 57 W. 57th St., New York.
Secretary: Dr. Benjamin Esterman, 983 Park Ave., New York.
Place: New York Academy of Medicine, 2 E. 103d St. Time: 8 p. m., first Monday of each month from October to May, inclusive.

Oklahoma City Academy of Ophthalmology and Otolaryngology

President: Dr. James P. Luton, 117 N. Broadway, Oklahoma City.
Secretary: Dr. Harvey O. Randel, 117 N. Broadway, Oklahoma City.
Place: University Hospital. Time: Second Tuesday of each month from September to May.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. D. D. Stonecypher, Nebraska City, Neb.
Secretary-Treasurer: Dr. W. Howard Morrison, 1500 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m. dinner; 7 p. m. program; third Wednesday of each month from October to May.

Passaic-Bergen Ophthalmological Club

President: Dr. Thomas Sanfacon, 340 Park Ave., Paterson, N. J.
Secretary-Treasurer: Dr. J. Averbach, 435 Clinton Ave., Clinton, N. J.
Place: Paterson Eye and Ear Infirmary. Time: 9 p. m., last Friday of every month, except June, July and August.

Philadelphia County Medical Society, Eye Section

President: Dr. Isaac Tassman, 136 S. 16th St., Philadelphia.
Secretary: Dr. Glen Gregory Gibson, 255 S. 17th St., Philadelphia.
Time: First Thursday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. George H. Shuman, 351–5th Ave., Pittsburgh.
Secretary: Dr. Robert J. Billings, 509 Liberty Ave., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Reading Eye, Ear, Nose and Throat Society

President: Dr. Michael J. Penta, 312 N. 5th St., Reading, Pa.
Secretary: Dr. Paul C. Craig, 232 N. 5th St., Reading, Pa.
Place: Wyomissing Club. Time: 6:30 p. m., third Wednesday of each month from September to July.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. Peter N. Pastore, Medical College of Virginia, Richmond, Va.
Secretary: Dr. Clifford A. Folkes, Professional Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

President: Dr. Frank Barber, 75 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. Charles T. Sullivan, 277 Alexander St., Rochester, N. Y.

St. Louis Ophthalmic Society

President: Dr. C. C. Beisbarth, 3720 Washington Blvd., St. Louis.
Secretary: Dr. H. R. Hildreth, 508 N. Grand Blvd., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting, 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmo-Oto-Laryngological Society

President: Dr. Belvin Pritchett, 705 E. Houston St., San Antonio 5, Texas.
Secretary-Treasurer: Lt. Col. John L. Matthews, AAF School of Aviation Medicine, Randolph Field, Texas.
Place: San Antonio, Brooke General Hospital, Randolph Field or San Antonio Aviation Cadet Center. Time: 7 p. m., second Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Roy H. Parkinson, 870 Market St., San Francisco.
Secretary: Dr. A. G. Rawlins, 384 Post St., San Francisco.
Place: Society's Bldg., 2180 Washington St., San Francisco. Time: Fourth Tuesday of every month except June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. David C. Swearingen, Slattery Bldg., Shreveport, La.
Secretary-Treasurer: Dr. Kenneth Jones, Medical Arts Bldg., Shreveport, La.
Place: Shreveport Charity Hospital. Time: 7:30 p. m., first Monday of every month except July, August and September.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. Clarence A. Veasey Sr., 421 W. Riverside Ave., Spokane, Wash.
Secretary: Dr. Clarence A. Veasey Jr., 421 W. Riverside Ave., Spokane, Wash.
Place: Spokane Medical Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. A. H. Rubenstein, 713 E. Genesee St., Syracuse, N. Y.
Secretary-Treasurer: Dr. I. H. Blaisdell, 713 E. Genesee St., Syracuse, N. Y.
Place: University Club. Time: First Tuesday of each month except June, July and August.

Toledo Eye, Ear, Nose and Throat Society

Chairman: Dr. E. W. Campbell, 316 Michigan St., Toledo, Ohio.
Secretary: Dr. L. C. Ravin, 316 Michigan St., Toledo, Ohio.
Place: Toledo Club. Time: Each month except June, July and August.

Toronto Academy of Medicine, Section of Ophthalmology

Chairman: Dr. W. R. F. Luke, 316 Medical Arts Bldg., Toronto, Canada.
Secretary: Dr. W. T. Gratton, 216 Medical Arts Bldg., Toronto, Canada.
Place: Academy of Medicine, 13 Queens Park. Time: First Monday of each month, November to April.

Washington, D. C., Ophthalmological Society

President: Dr. Harold M. Downey, 1740 M St. N. W., Washington, D. C.
Secretary-Treasurer: Dr. Richard W. Wilkinson, 1408 L St. N. W., Washington, D. C.
Place: Medical Society of District of Columbia Bldg., 1718 M St. N. W., Washington, D. C. Time: 7:30 p. m., first Monday in November, January, March and May.

Wilkes-Barre Ophthalmological Society

Chairman: Each member in turn.
Secretary: Dr. Samuel T. Buckman, 70 S. Franklin St., Wilkes-Barre, Pa.
Place: Office of chairman. Time: Last Tuesday of each month from October to May.